The Journal of Thoracic Surgery

VOL. 24 OCTOBER, 1952 NO. 4

Original Communications

TRAUMATIC SACCULAR ANEURYSM OF THE THORACIC AORTA

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TRAUMATIC saccular aneurysm of the thoracic aorta is apparently rare. Few cases are reported in the literature; no patients reported have survived more than eleven months, and all have been diagnosed at autopsy. This report is based on four patients, diagnosed during life, who have survived from a few months to seven years following their injury. In one case the development of the aneurysm was observed by serial roentgenograms. Correlating our observations with a study of the mechanism and pathology involved in traumatic rupture of the aorta has led to certain conclusions: (1) that this condition may occur far more frequently than is supposed; (2) that incomplete rupture of the aorta may possibly be diagnosed early and definitive treatment of the rupture instituted; (3) that if the aneurysm is already forming or has formed treatment to prevent further enlargement or later rupture may be carried out.

CASE 1.—L. F., a 27-year-old white man, was admitted to the hospital on Sept. 29, 1949, with a history of having been involved in an automobile accident six days previously. He had been unconscious following the accident and hospitalized elsewhere. He had received multiple abrasions and lacerations, injury to the left forearm and hand, and severe contusion of the chest. There had been some coughing up of blood on the first day after injury. At the time of admission here the only complaint referable to the chest was occasional pain in the chest when coughing or on deep breathing.

Other than the residuals of the trauma, physical examination was essentially negative. Some dullness was noted on the left side of the chest posteriorly to about the level of the eighth rib. There was tenderness of the left wrist on motion.

Routine laboratory tests were within normal limits except the Kahn, which was reported positive, 32 Kahn units. This test was repeated a week later with the same result. The spinal fluid Kahn was negative. A repeat Kahn in one month was reported positive, 8 Kahn units. Four days later the result was doubtfully positive, 0 Kahn units, and within three

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Reviewed in the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are the result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

Read at the Thirty-second Annual Meeting of The American Association for Thoracic Surgery, Dallas, Texas, May 8-10, 1952.

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weeks the report was negative. In view of a negative history of a primary lesion and the rapidity with which the Kahn test became negative (no treatment was given), it was the opinion of our medical consultant that it was unlikely that this man had syphilis.

Roentgenogram of the left forearm and hand revealed a fracture of the ulna and of the proximal phalanx of the ring finger. A film of the chest on September 30 showed clouding over the left base, which was interpreted as fluid.

The fractures received appropriate treatment, and thoracentesis of the left chest produced about 75 c.c. of blood. In a few days the patient was ambulatory, but he remained in the hospital for treatment of his fractures. Repeat chest roentgenograms were made on October 4 and 11, and on the latter date there was no further evidence of fluid. (Discussion of all roentgenograms will follow the completion of the case history.) On December 18 a

Fig. 1.—Case 1. Saccular aneurysm as seen at operation.

repeat roentgenogram of the chest was made before the patient was to go on a Christmas pass. It was at this time that a definite mass was seen in the region of the aortic knob, and further studies, including fluoroscopy, were done. Pulsation of this mass was seen, but it could not be determined whether or not it was transmitted. Following his return to the hospital early in January, roentgenograms of the chest indicated that the mass had continued to enlarge, and angiograms were made. These showed conclusively that the mass represented an aneurysm of the first portion of the descending aorta.

Operation was advised, and on Feb. 2, 1950, the chest was explored through the bed of the resected fifth rib. Except for adhesions of the lung to the aneurysm, the pleural cavity was free. These adhesions were carefully freed by blunt and sharp dissection and the aneurysm exposed (Fig. 1). No pulsations could be seen, and the wall felt quite firm. The

upper limit was approximately 5 cm. distal to the subclavian artery take-off, and it gave the appearance of a large bulge on the lateral side of the aorta. The aneurysm was well localized to the lateral wall, and it was felt that local covering with Cellophane would be sufficient. A flap of pleura was freed from the base of the entire aneurysmal area, and a piece of sclerosing type of Cellophane was sutured to the flap, completely covering the lesion. This in turn was covered by a sheet of nonsclerosing Cellophane to protect the lung. Closure was routine, with one catheter as a drain, connected to an underwater seal. Recovery from the operation was uneventful, but discharge from the hospital was delayed so that the patient could receive physiotherapy for the arm and hand fractures.

Follow-up has been regular at six-month intervals and, except for clearing of pleural reaction, there has been no change in the lesion. However, on Jan. 24, 1952, the patient was readmitted, complaining of a constant dull pain referred through from between the shoulders posteriorly to the precordium anteriorly. He had been doing heavy work running an air compressor for the past six months. Fluoroscopy and roentgenogram, including angiogram, revealed no change in the lesion (Fig. 8). Following three weeks' rest in the hospital he improved and was discharged, being strongly advised to seek less laborious work.

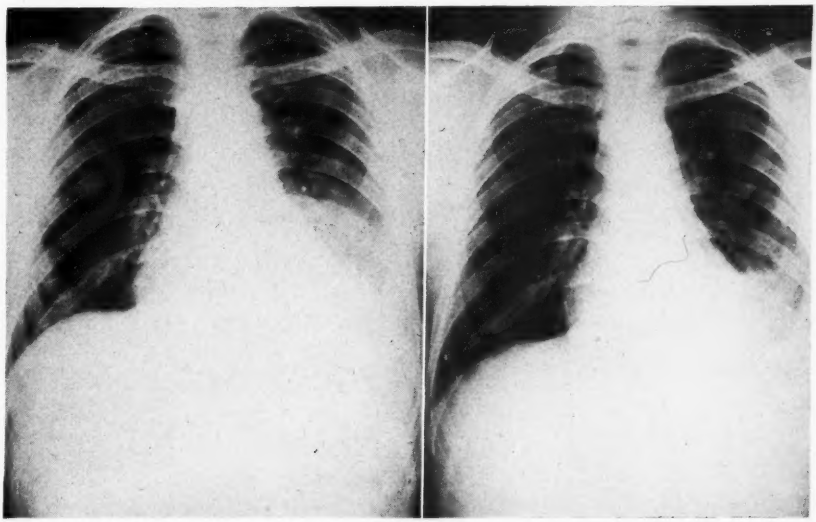

Fig. 2. Fig. 3.

Fig. 2.—Case 1. Admission roentgenogram, Sept. 30, 1949, one week after accident. Note widening of mediastinum.

Fig. 3.—Case 1, Oct. 4, 1949. Little change except clearing of pleural fluid.

Discussion.—Fig. 2 shows the initial chest roentgenogram. In addition to the evidence of pleural fluid, you will note the narrow band of increased density just to the left of the heart shadow. No significance was attached to this in the initial reading. Strassmann found that, in eight cases with partial rupture of the aorta at this site, the patients lived three or more hours, and at autopsy a tear was found extending through all coats of the vessel except the adventitia. There was dissection of blood along the aortic wall between the adventitia and media. In retrospect, we believe that this shadow represents widening of the aorta due to dissection. Strassmann's patients died of shock

or other effects of their injury. Our patient fortunately survived the immediate trauma, and in Figs. 3 and 4 we see further developments. These are roentgenograms taken four days and eleven days, respectively, after Fig. 2, and we see a change in this shadow, with the lesion becoming more localized at the site of the tear, and probably absorption of some of the dissecting blood. While this shadow was noted in the original roentgenographic report, its significance was still not recognized. However, in the film taken approximately one month later (Fig. 5) there is little room for doubt. We felt that we were dealing with aneurysm, probably of the aorta, and that angiograms should be made. In spite of our advice and explanations of the danger involved, the patient insisted on waiting until after Christmas. On his return to the hospital early in January, roentgenographic studies indicated still further enlargement of the mass (Fig. 6), and angiograms (Fig. 7) proved conclusively that we were dealing with an aneurysm. Operation was advised and accepted. Fig. 8 shows the roentgenographic appearance of the lesion two years after operation.

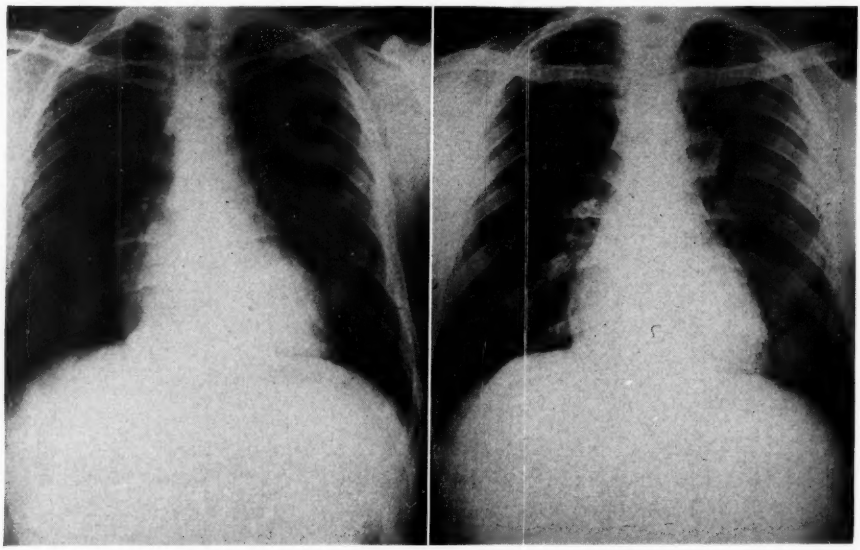

Fig. 4. Fig. 5.

Fig. 4.—Case 1, Oct. 11, 1949. The sac is beginning to form.
Fig. 5.—Case 1, Dec. 16, 1949. Sac is enlarging.

CASE 2.—S. L. W., a 27-year-old white man, was admitted to Kennedy General Hospital on Jan. 25, 1945. He had been injured in an ambulance accident in Paris, France, on Nov. 27, 1944. These injuries resulted in paraplegia from the level of L4. All laboratory reports were within normal limits. The history revealed that at the time of the accident a roentgenogram of the chest showed considerable wedging of the mediastinal shadow which could be due to mediastinal hemorrhage. Following a repeat film two weeks later it was reported that this mediastinal enlargement had disappeared. On Jan. 15, 1946, a routine chest roentgenogram was reported as showing a localized small density in the left superior mediastinum which was thought to be either a small dermoid cyst or lymph node enlargement

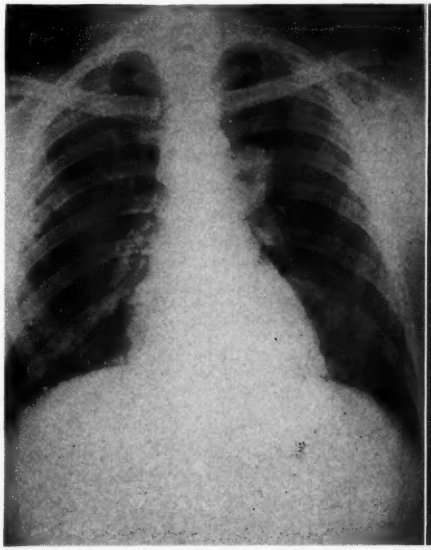

Fig. 6.

Fig. 7.

Fig. 6.—Case 1, Jan. 31, 1950. Preoperative film. Size of aneurysm has increased slightly.

Fig. 7.—Case 1, Jan. 13, 1950. Angiogram showing aneurysm.

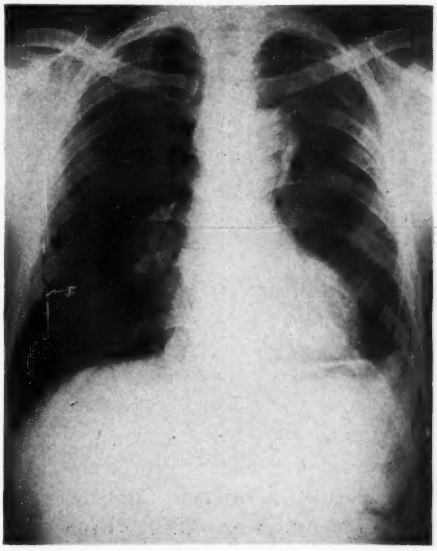

Fig. 8.—Case 1, Jan. 24, 1952. Checkup film two years after operation.

(Fig. 9). On May 25, 1946, an exploratory thoracotomy revealed this mass to be an aneurysm, 5 cm. in diameter, projecting from the lateral wall of the first portion of the descending aorta. The chest was closed, and recovery was uneventful. He was discharged from the hospital on Aug. 7, 1946. There were no chest symptoms.

Discussion.—From the record available we have no report of chest roentgenograms from December, 1944, to January, 1946. The mediastinal shadow appearing in the initial film cleared rather rapidly, indicating that it probably represented mediastinal hemorrhage. Just when the aneurysm first became visible or how fast it enlarged is unknown. It is suggested that in all cases of severe chest trauma, particularly if there has been any evidence of widening of the

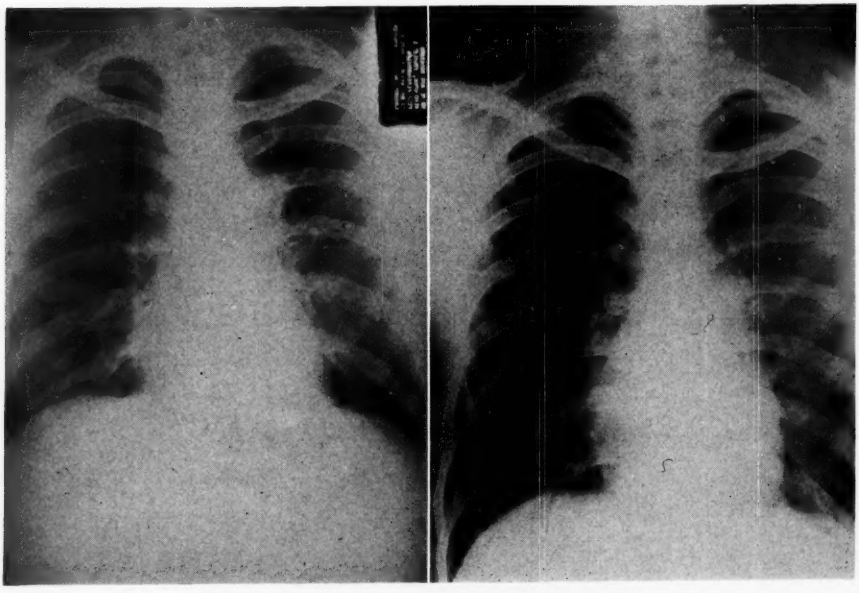

Fig. 9. Fig. 10.

Fig. 9.—Case 2. Preoperative film.
Fig. 10.—Case 2. Induction film; no evidence of aneurysm.

mediastinal shadow, repeat roentgengrams should be made during the first two or three months. Fig. 9 shows this lesion preoperatively. Fig. 10 is the induction film taken in 1941. No aneurysm is visible. Fig. 11 is a checkup film taken in August, 1951. No definitive treatment was given, and it would be interesting to know if it would have been wrapped with Cellophane had that material been available at that time.

This patient has remained well and without symptoms or evident enlargement for over seven years after his accident. But he is a paraplegic and has been relatively inactive. Occupation may play a part in the late development of symptoms or rupture.

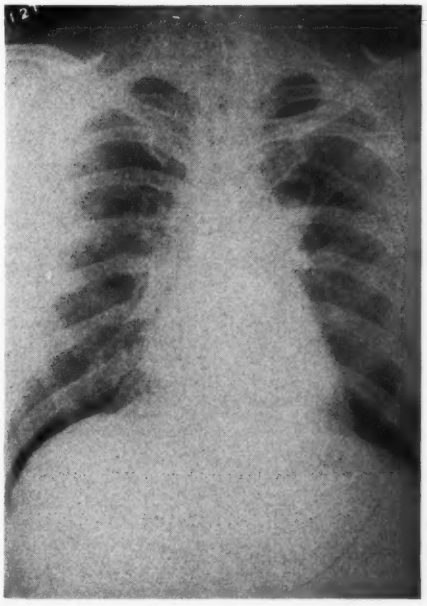

Fig. 11.—Case 2. Seven years after injury.

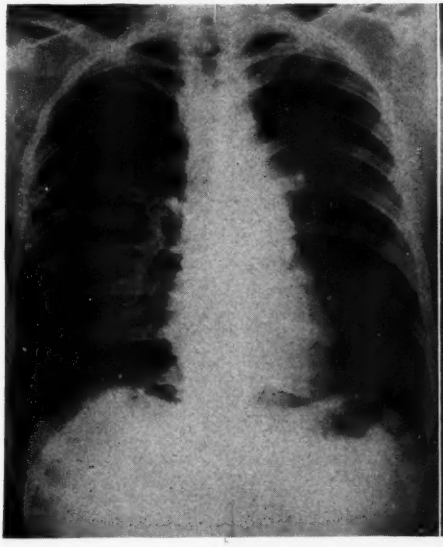

Fig. 12. Fig. 13.

Fig. 12.—Case 3, Jan. 30, 1950. Routine separation film.
Fig. 13.—Case 3, June 10, 1950. Last checkup five months postoperative. Note increase in size.

CASE 3.—This patient was a 19-year-old soldier whose lesion was discovered on routine separation chest roentgenogram in January, 1950 (Fig. 12). On fluoroscopy there was some pulsation of the mass, but it could not be determined whether this was actual or transmitted. On barium swallow the esophagus was seen to be displaced slightly to the right and posteriorly. Physical examination was negative. All laboratory data, including serology, were negative.

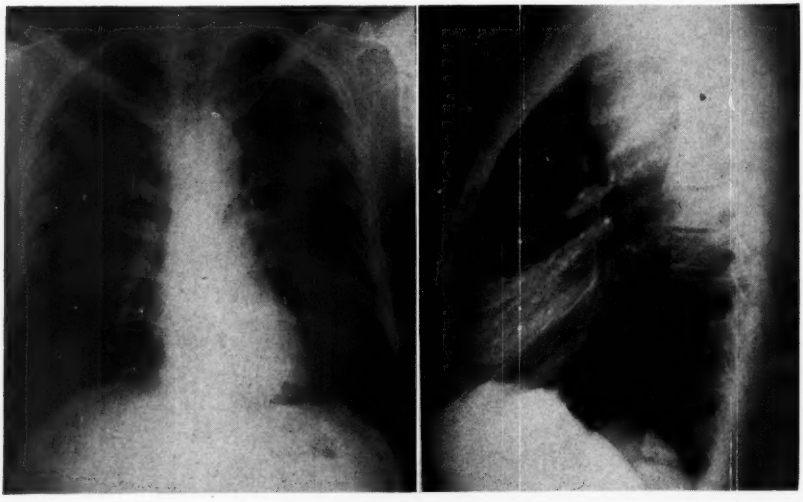

Fig. 14. Fig. 15.

Fig. 14.—Case 4, Jan. 5, 1952. Initial film posteroanteriorly.
Fig. 15.—Case 4, Jan. 5, 1952. Lateral showing mass and fracture of sternum.

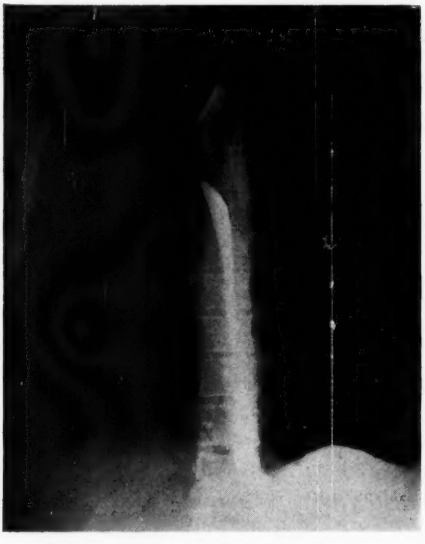

Fig. 16.—Case 4. Barium swallow.

The only significant feature of his history was that he had been involved in a jeep accident approximately one year previously. No chest films were available from that accident. The chest roentgenogram on his admission to the army was thought to be negative, but it was not available.

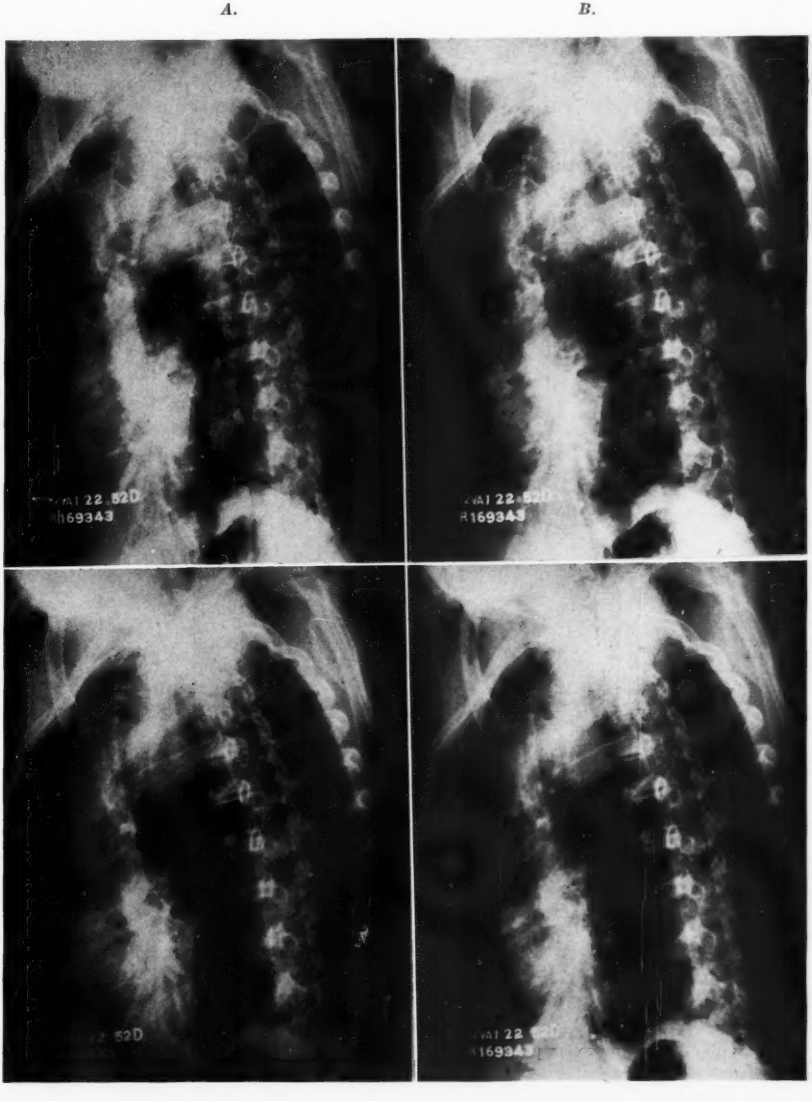

Fig. 17.—*A*, Case 4. Angiocardiogram, eight and one-half seconds. *B*, Ten seconds. *C*, Thirteen seconds; note dye pooled in aneurysm. *D*, Seventeen and one-half seconds; dye still pooled in aneurysm.

Left exploratory thoracotomy was performed on Feb. 15, 1950, and a large saccular aneurysm of the first portion of the descending aorta was found. The chest was closed. On March 22, 1950, the left chest was again explored with the idea of excising the aneurysm. However, it was thought to be too extensive. Furthermore, the thinnest portion was so densely adherent to the pulmonary artery, bronchus, and vein, it was thought that dissection would be entirely too hazardous.

Postoperatively there was considerable difficulty in re-expanding the left lung, but he was finally discharged from the hospital on May 11, 1950. The last roentgenogram was in August, 1950 (Fig. 13). It shows that this mass was definitely larger.

Discussion.—Here is an otherwise healthy young man who had been in a severe accident one year previous to the finding of a large saccular aortic aneurysm. While no pre-accident roentgenogram is available, it is reasonable to assume that he had no such mass when inducted into the army, and we are accepting it as a true traumatic saccular aneurysm of the aorta.

Fig. 18.—Case 4, Feb. 21, 1952. Note increase in size of aneurysm.

Cellophane wrapping was considered at the first operation and, had it been available, might have been used. The only follow-up available is contained in a letter and reported by Dr. Paul to the effect that one year after leaving the hospital he is apparently "all right." Further follow-up is important in this case, and every effort will be made to obtain it.

CASE 4.—M. W. A., a 33-year-old white man, was admitted to Mt. Alto Hospital, Washington, D. C., on Dec. 28, 1951. The chief complaint was substernal pain which was increased by swallowing. This had been present since an automobile accident on Dec. 15, 1951, at which time he was struck in the chest by the steering column of his car. He was unconscious for about two hours, and suffered numerous minor cuts and abrasions. The substernal pain, aggravated by swallowing, had been constant. It was knifelike, and occasionally radiated through to the thoracic spine. Following one week of hospitalization he was discharged, returned to Washington, and had a chest roentgenogram taken at Arlington Hospital. He was told that he had a mass in the posterior superior mediastinum, and that this mass most likely represented a hematoma.

Physical examination was essentially negative except for tenderness over the sternum at the level of the third costal cartilage. The trachea was deviated slightly to the right. All laboratory examinations were within normal limits, except the urine and blood sugar. This man was a known diabetic.

Posteroanterior roentgenogram of the chest (Fig. 14) taken on Jan. 5, 1952, demonstrated widening of the superior mediastinum. The lateral film shows this mass to be somewhat posterior, and that there is a fracture through the middle of the sternum (Fig. 15). A barium swallow revealed a mediastinal mass with displacement of the trachea and esophagus (Fig. 16). Angiocardiograms revealed an aortic aneurysm arising from the left aspect of the transverse arch (Fig. 17, *A, B, C, D*). A film taken on Feb. 21, 1952 (Fig. 18), showed a moderate but definite increase in the size of the aneurysm. A chest roentgenogram taken at Perry Point Hospital seven months previously was reviewed, and no evidence of a posterior superior mediastinal mass was noted.

Thoracic surgery consultation was obtained and a diagnosis of traumatic aneurysm of the aorta was made. No treatment was recommended and the patient was advised to have a chest roentgenogram once a month. The hospital course was uneventful and the patient was discharged on Jan. 31, 1952.

Discussion.—There is no question but that this is a traumatic aneurysm. An interesting feature is the location, which is somewhat unusual. Here, instead of the usual indirect cause of aortic laceration (discussed later), we probably have a direct injury from a caving in of the sternum against the underlying aorta. The lesion showed definite evidence of increase in size during the hospital stay. Our knowledge of the ultimate outcome of this type of lesion without treatment will be enhanced by a careful long-term follow-up.

LITERATURE

Blunt force injuries to the chest may cause a variety of intrathoracic injuries to the heart or great vessels. Rupture of the heart, a heart valve or the aorta, purulent pericarditis, chronic adhesive pericarditis, mitral stenosis, and aneurysm of the heart are some of the results of trauma reported in the 126 cases collected by Bernstein.[1] He found that the first case of traumatic aneurysm was reported by Lesta in 1813. However, the report of this case would indicate that it was an aneurysm of the heart.

Traumatic rupture of the aorta is probably of more frequent occurrence than reports in the literature would indicate. Case reports by McDonald and Campbell,[2] Jaffe and Sternberg,[3] Shennan,[4] Landau,[5] Kemp,[6] Busse,[7] and others have appeared from time to time. Strassmann[8] reports that, from approximately 7,000 autopsies performed during the six years from 1936 to 1942 at the Chief Medical Examiner's Office of New York City, seventy-two cases of traumatic rupture of the aorta were collected. Of the sixty-one who had only one site of rupture all but three were in the thoracic aorta. Mennyey[9] reports a series of cases of aortic wounds with survival. Most were in the thoracic aorta but were caused by penetrating injuries. No late survival with aneurysm was mentioned.

Of much less frequency are reports of traumatic aneurysm of the thoracic aorta, first mentioned by Versalius[10] over three centuries ago. Aschoff's case, cited by Stern,[11] was of the dissecting type, was in the ascending aorta, and was due to a gunshot wound. He survived the injury for four months. Leonard[12]

reports a patient 60 years of age who survived a crushing chest injury for sixteen days. At autopsy a dissecting aneurysm of the ascending aorta was found. Samson[13] also reported a dissecting type of aneurysm of the descending aorta attributed to an acident five years previously. Hübener's[14] case followed an automobile accident. It is impossible, from reading the case history, to be sure whether it was a saccular or dissecting type. Moxon[15] (1870) reports one case and Albutt[16] (1870) two cases diagnosed as traumatic aneurysm of the thoracic aorta. All three were diagnosed from clinical signs suggesting that they were located in the ascending aorta. Their traumatic origin was based on the fact that in each instance the patient was described as in excellent health before severe chest injury, and the aneurysm was diagnosed shortly thereafter.

Heller,[17] in 1903, writes of a man 37 years of age who had a heavy mass fall on his chest. He died eleven months later, and autopsy revealed a saccular aneurysm of the first portion of the ascending aorta. Kaufmann[18] reports seeing a "saccular aneurysm as large as a walnut in the thoracic part of the otherwise perfectly healthy aorta of a sturdy young man. It had developed some months after a severe fall." No further information is given. Shennan[4] cites a case of a man of 57 years who died eight weeks after being knocked over by a bicycle. He died suddenly with a severe hematemesis. Autopsy revealed rupture of the thoracic aorta at the level of the fifth intercostal artery opening into an aneurysm which had in turn eroded into the esophagus and ruptured. Shennan calls this a false aneurysm, which classification is difficult to accept in view of the poor quality of the tissues which would of necessity form the aneurysmal wall in this area. Spearman and Nissen's[19] cases were both due to gunshot wounds. Spearman's was in a 19-year-old boy who died from rupture and Nissen's in a 36-year-old man who was still alive after nine years. Stryker[20] in 1948 reports the case of an 18-year-old girl who was injured in an automobile accident five months before her death. At autopsy one large (4 cm. by 5 cm.) saccular aneurysm was found in the first portion of the aorta just above a cusp of the aortic valve. There was also a smaller defect on the opposite wall. Stryker also reports two cases from the records of the Department of Pathology of the University of Michigan in which death occurred shortly after severe trauma and in which there was incomplete tearing of the aorta. He believes this to be a first stage in the development of traumatic aneurysm.

DISCUSSION

Traumatic saccular aneurysm of the aorta may be due to blunt trauma to the chest or to penetrating wounds. This discussion is limited to the former. In addition, greater stress is laid on those lesions involving the first portion of the descending aorta. This is the most frequent site and the only one with which we have had any experience. Of no less importance are those occurring in the first portion or ascending aorta, and any further study of these lesions should, if possible, include both sites.

By definition[21] a true aneurysm is one in which the sac is formed by the arterial walls, one of which, at least, is unbroken; and a sacculate aneurysm is a saclike arterial dilatation which opens into the artery by an opening that is

small compared to the size of the sac. We believe that the aortic lesions under discussion are true sacculated aneurysms. They are a result of injury to that organ. The mechanism of formation is in direct relation to the degree of disruption of the aortic wall. Complete rupture means instant death. If the intima only is torn, a dissecting aneurysm may form or healing may occur, as Peery[22] has shown in cases of spontaneous rupture. If both the intima and media are ruptured, leaving only the adventitia, and death does not occur from other results of the accident, an aneurysm may form. To understand the mechanism of the formation of these aneurysms, therefore, one must study aortic rupture.

Most authorities believe that the arterial system, if healthy, is able to withstand, without rupturing, any conceivable increase in blood pressure which can be produced by a strongly contracting left ventricle during great temporary physical or mental strain. Klotz and Simpson[23] were unable to rupture the aorta of individuals from 20 to 40 years of age with pressures up to 1,000 mm. of mercury, while Oppenheim[24] reported rupture at a pressure of 3,000 mm. of mercury. It is therefore difficult to accept the theory that an increase in intra-arterial pressure causes a bursting rupture from within. However, it must be borne in mind that a *sudden* change in pressure will have greater effect than a continuous force,[25] and it is possible that this is a contributing factor. Obviously, other more important factors must be considered, and several theories have been advanced.

It is important, at this point, to consider the usual site of rupture. All reported aneurysms and practically all ruptures were at one of two sites, the first portion of the ascending aorta or the beginning of the descending aorta just distal to the ligamentum arteriosum. Strassmann's series, the largest reported, showed that in thirty-eight of sixty-one cases the rupture was in the latter location. As both of these sites are also those of predilection for spontaneous dissecting aneurysm, it must be agreed that they represent "weak" areas in what is usually considered a "tough organ." Both the first portion of the ascending aorta and the beginning of the descending aorta are comparatively fixed points, the former by the fibrous union between the aorta and the pulmonary artery, and the latter by the ligamentum arteriosum and the large vessels.

According to Warfield[26] the mechanism in injuries to the heart and the proximal portion of the aorta or the root is that in full inspiration sudden compression of the chest finds the heart caught and held between the inflated lungs. A violent blow on the chest, whether over the heart or not, may injure the heart, particularly if it is in diastole. It may rupture the myocardium, a valve, or the root of the aorta. Peery[22] states that the valve commissures exert a rocking force and pull on the aortic wall as they are driven shut in diastole by the column of aortic blood, and this local force is probably the cause of the more frequent occurrence of tears at this point. The fact that the tears are usually transverse to the axis of the valve commissures adds weight to this hypothesis. While he was speaking particularly of spontaneous tears, Peery's theory appears valid in conjunction with that of Warfield in cases of traumatic rupture in this area.

Strassmann believes that the majority of traumatic ruptures develop at the isthmus of the aorta because of the fact that the aorta is narrowed and relatively fixed at this site by the attachment of Botallo's ligament. This might render this portion of the vessel more subject to overextension or twisting or sudden increase in intra-arterial pressure.

According to Hass,[27] "whenever one part of the body is decelerated at a rate which is different from that of another part . . . the connection between these parts is placed under stress which is proportional to the rates of deceleration." Rice and Wittstruck[28] have described their concept of the mechanism and shown it diagrammatically as reproduced in Fig. 19. According to these authors, "in linear deceleration of the thorax, the central portion of the descending aorta, being the least rigidly bound, is snapped forward by the momentum of the deceleration force and the mass of the aorta's content of blood. This force is irregularly absorbed by the elasticity of the vessel and the thoracic contents . . . . the upper portion of the aorta is most rigidly fixed by the great vessels of the arch and the ligamentum arteriosum. This portion decelerates at the same rate as the whole body, while because of its less rigid fixation the descending aorta decelerates at a different rate. This difference constitutes the force which is concentrated at the point of maximum fixation."

It has been suggested that the area just distal to Botallo's ligament, being the usual site of coarctation, may be an embryologically weak point in the aorta, but no substantiating pathologic evidence has been shown. According to Abbott,[29] weakness at this point is usually associated with other vascular abnormalities.

Stryker[20] gives the only complete pathologic description of a traumatic aneurysm. Fig. 20 is a cross section of the larger aneurysm in his first case. "The interrupted elastic fibers formed a tangled mass at the edge of the lesion, and there were scattered individual elastic fibers and small masses of fibers in the walls and floor." There was an organizing thrombus attached to a portion of the wall. An additional interesting and important pathological finding was the presence of subacute bacterial endaortitis.

TREATMENT

Obviously, from this small series of cases, no dogmatic statement regarding the proper treatment of these serious lesions can be made. As a matter of fact, with each case encountered, a different problem was presented, and we became more confused. Out of this confusion we have attempted to draw some valid conclusions but at this point we can only theorize and then place the matter before you for discussion and further consideration.

The treatment followed will vary with the stage of development of the aneurysm. Arbitrarily we have divided this into three stages. We believe, with Stryker, that there is a first or pre-aneurysm stage. Here we have the laceration of the inner two coats of the aortic wall and a varying degree of dissection. That stage is well demonstrated in Fig. 2. Strassmann showed this in the eight cases of his series who had incomplete rupture. If, at this stage,

the patient's condition permits, exploratory thoracotomy with suture of the lacerated aorta may be feasible. Dshanelidze,[30] Blalock,[31] Elkin,[32] and Beattie[33] have all reported successful suture of a lacerated aorta. The difficulty here is twofold: (1) early diagnosis is essential and admittedly difficult; (2) unfortunately many, if not most, of these patients will be in serious condition from other injuries and not immediately operable. The duration of the first stage is undoubtedly short.

Referring to Fig. 3, taken two weeks after the accident, we see little change from Fig. 2. However, in Fig. 4 there is definite beginning formation of a sac. We assume from this that the first stage in this case continued for approximately two weeks. Should suture of the laceration not be possible, wrapping the area with Cellophane of the Polythene type, as recommended by Poppe and de Olivera[34] for syphilitic aneurysms, is suggested. This might prevent formation of the sac or at least produce enough reaction to limit its size.

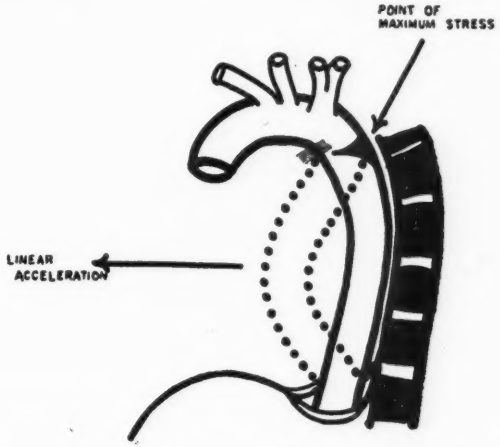

Fig. 19.—Diagrammatic representation of the mechanism of laceration of the healthy aorta by indirect violence. (From Rice and Wittstruck: J. A. M. A., Nov., 1951.)

During the second, or developmental stage, as exemplified by Figs. 4 and 5, operation should be performed as soon as the condition of the patient permits. Here one of two procedures might be carried out. From the evidence available the wall of the sac consists of the adventitia, the opening into it varying with the size of the laceration. While the sac is still small it might be possible to resect it and then suture the laceration. A more conservative approach would be Cellophane wrapping. This should prevent further increase in size and reduce the possibility of rupture.

The third, or late stage, will comprise those cases seen months or years after the accident, most probably seen on roentgenograms taken routinely or for other causes, as in Cases 2 and 3 of this report. There may possibly be symptoms present as in Nissen's case, reported eleven years after a bullet wound received in World War I. While the actual cause of this aneurysm was different

from those under discussion, it gives us an insight into possible late results and thus might well influence the choice of treatment. Because it represents the longest known survival of a patient with a traumatic aneurysm, we feel that a brief mention of the symptoms is in order. They consisted of pressure feeling in the chest which increased to dyspnea on exertion, some cough with scanty expectoration, pains which radiate to the left arm, and disagreeable sensations in the area of the heart. These symptoms had increased considerably during the preceding two years, and Nissen felt that this was probably due to an increase in size of the lesion.

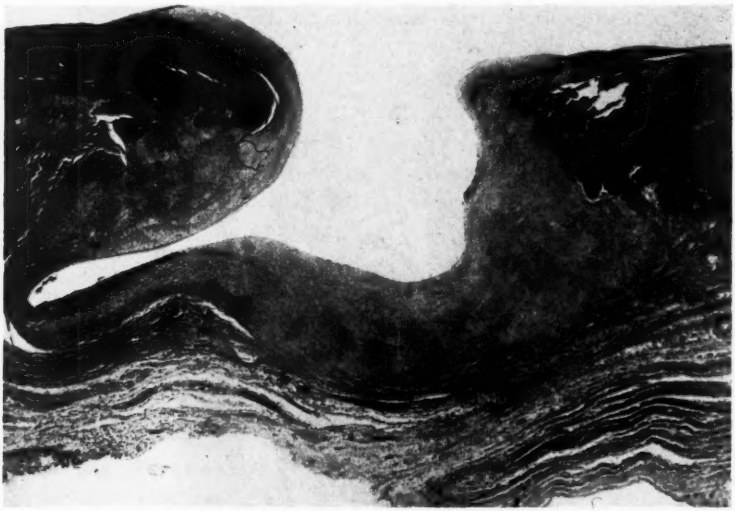

Fig. 20.—Section through saccular aneurysm, elastic tissue stain. See text. (From Stryker, Am. J. Clin. Path., Feb., 1948.)

Whether or not surgical therapy should be recommended in this stage might depend on three factors: (1) the age of the aneurysm, (2) the age and occupation of the patient, and (3) the presence or absence of symptoms. Certainly with an aneurysm of considerable age, symptomless and in a patient with a more or less sedentary occupation, one might advise against surgery. But just when can a traumatic aneurysm be deemed old enough to be considered stable? In Case 3 we see rather marked enlargement, following exploration of the chest, in a lesion over a year old. Here occupation enters into the picture. Heavy labor is much more likely to be a cause of enlargement, symptoms, or even rupture, than light desk work. We believe very heavy labor to be contradicted, regardless of whether the lesion is treated or not. For the various gradations of work between that and a sedentary life, active treatment must be given very serious consideration. It is not enough to advise frequent chest roentgenograms, watching for a change in size, because any change may be so sudden and extensive as to quickly carry the case beyond help. Case 2 has gone seven years

without symptoms or change in the size of the aneurysm, but the patient is a paraplegic and has perforce led a sedentary life. Symptoms, if present, call for surgical interference. Nissen,[19] in 1927, suggested that surgical interference should be considered in his case and should consist of transplantation of fascia around the wall, or, if the stem of the sac was small, extirpation.

The conservative treatment consists of Cellophane wrapping. We have no knowledge of the long-term results with this substance in this type of lesion, but the results in some syphilitic aneurysms are encouraging enough to warrant a thorough trial. Our patient has now gone two years with no increase in size of his lesion (Fig. 8), but he has recently been hospitalized for study because of symptoms which conceivably could be due to the aneurysm. He had been operating a large pneumatic drill for the past six months, which may have caused his symptoms even if he had no aneurysm. Extensive studies, including an angiogram, were negative. He will report to us later after doing lighter work.

In patients in whom the lesion is diagnosed at an exploratory operation, we feel that wrapping should be done. It adds little to the procedure, and may prevent future trouble.

With our present meager knowledge of all phases of these lesions, we do not feel justified in recommending the more radical procedure of resection and grafting. Few clinics in the country have the blood vessel bank needed, the procedure is a formidable one, and until the more conservative treatment has been definitely proved inadequate, we believe that resection will be rarely indicated.

CONCLUSIONS

With the many crushing blows encountered in the ever-increasing accident rate, and with improvement in diagnosis and treatment of intrathoracic lesions, the early recognition of traumatic aneurysm becomes more and more important.

We would like to point out that a small density following parallel and outside the descending aorta was the first sign noted in Case 1. In the beginning, due to hemothorax, we interpreted the parallel density as pleural blood or fluid and no more significance was attached to it. As the shadow became larger and more dense, the exact meaning was not known until the outlines began to become sharp, and then aneurysm was considered.

In the development of densities along the left paramediastinum between the transverse aorta and hilum, many different causes must be considered. Katz and Reed[35] point out the possibility of paramediastinal pleural effusion which we first suspected. However, lymphoblastoma and superior and posterior mediastinal tumors, in various stages of growth, may give a similar picture, as seen in the first and third cases.[36] We have recently seen a case of a benign thymoma which presented a shadow almost identical to these two cases (Cases 1 and 3).

It is interesting to note that three of the four cases presented here have almost identical roentgenographic findings. This may be of aid in future diagnosis of this type of case.

Angiograms have been of great value in making a correct diagnosis[37] when the condition of the patient permits. Fluoroscopic examination may or may not give additional information, but we feel it should be used as an adjunct diagnostic aid.

We believe that active treatment is indicated in most cases if it can be accomplished without unduly adding to the risk, and, until more is known of the ultimate outcome under normal conditions of living, this should consist of Cellophane wrapping. As mentioned earlier, our knowledge is too meager to be dogmatic, but it is logical to assume that no surgeon could sit idly by, watching an aortic aneurysm grow larger and larger, unless his considered judgment dictated that the risk of surgery was far greater than the lesion per se.

That a great deal of further observation and study is required is obvious, and it is to be hoped that the reporting of this small series of cases will stimulate this study. Such a study should include (1) extensive autopsy study of cases following severe chest injury, with particular reference to aortic trauma when death has been delayed and was not due to the aortic lesion; (2) autopsy study in all possible cases who die suddenly months or years following severe chest injury; and (3) careful roentgenographic follow-up of all patients who have severe chest trauma but in whom no immediate residuals are evident. It is probable that many serious internal injuries are unrecognized, the obvious injuries such as fractures, etc., directing attention away from the "silent" injury. Thousands of people are injured daily. There should be plenty of material for study.

We are indebted to Dr. Felix Hughes and the Kennedy General Hospital, Col. John Paul and the Walter Reed Hospital, and Dr. Louis Alpert and Mt. Alto Hospital for the use of Cases 2, 3 and 4, respectively; to Dr. Walter Stryker, Dr. S. E. Gould, Editor, *American Journal of Clinical Pathology*, and the Williams and Wilkins Company for permission to reproduce Fig. 20; to Dr. Walter G. Rice, Dr. Kenneth P. Wittstruck, and the *Journal of the American Medical Association* for permission to reproduce Fig. 19; to the Department of Medical Photography at Mt. Alto Hospital for the figures of Case 4; and to the Veterans Administration Regional Office at Albany, N. Y., for the follow-up on Case 2.

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DISCUSSION

DR. DENTON A. COOLEY, Houston, Texas.—Despite the fact that numerous procedures have been suggested and advocated for treatment of anuerysms of the aorta, for the most part the results of such surgical techniques have proved to be unsatisfactory. With regard to the cases just presented, it appears worth while to call attention to a more direct and definitive technique in management of such lesions, emphasizing a fundamental principle of surgery, namely, the excision of destroyed tissue.

An experience with a small group of patients with aneurysms of the thoracic aorta and its tributaries has emphasized to us the practicability of excisional therapy in aneurysms so situated.

(Slide.) A patient aged 37 years with coarctation of the aorta was admitted to the Johns Hopkins Hospital early in 1950 because of severe pain and pulsations in the right supraclavicular region. The coarctation was successfully resected by Dr. Blalock. About eight weeks later the patient was readmitted for exploratory thoracotomy on the right side.

At operation an extensive saccular aneurysm of the first portion of the right subclavian artery was excised. Encouraged by the result obtained from excision of a large aneurysm, I used this technique on a patient with a syphilitic aneurysm of the innominate artery.

(Slide.) The aneurysm arose from the arch of the aorta. The broad base of the aneurysm was occluded with a Crafoord clamp, and the aneurysm was excised. Lateral aortorrhaphy was done with a double row of silk sutures. The aortic tissue in this patient with syphilitic aneurysm was tough and leathery and held sutures well.

(Slide.) In this patient, a 54-year-old man, there was a syphilitic aneurysm of the ascending aorta and of enormous size. The lesion was completely excised, and lateral aortorrhaphy accomplished to the 10 centimeter aortic defect. This patient died eighteen hours later, probably of cerebral anoxia, most likely an anesthetic complication related to the bilateral open thorax at operation. The first and second patients are alive and doing well.

In reported analyses of large series of aneurysms of the aorta, one is struck by the alarmingly high expected mortality. This feature of the problem places aneurysm, together with carcinoma, in the group of highly fatal diseases. An aggressive approach to such lesions by thoracotomy and attempted removal therefore is justifiable. An important feature in our cases of aneurysmectomy was a relatively pliable and elastic aortic wall suitable for suture. This is characteristic of syphilitic aneurysms, particularly in the relatively young patient. A traumatic aneurysm, such as illustrated by Dr. McCooey, and similar to my case of subclavian aneurysm, may likewise occur to an otherwise healthy aorta, and would, therefore, be suitable for suture techniques. On the other hand, aneurysms of an arteriosclerotic nature are probably not amenable to this type of therapy.

DR. RALPH A. DETERLING, JR., New York.—We have been fortunate at Presbyterian Hospital in New York to have the pioneering efforts of Dr. Blakemore lead us through various evolutions of treatment of aneurysms of the aorta. As has been mentioned, most of those of the thoracic aorta that we encounter are syphilitic. With this type the wall of the aorta adjacent to the lesion may lend itself very nicely to suture technique. Dr. Blakemore and those of us who have applied plasticized polythene or fibrosing Cellophane to the actual sacs have considered our over-all results with this technique not too satisfactory. We know of several cases in which the aneurysm has been fairly well controlled, but the aorta has ruptured above the area where the Cellophane was applied. This is a hazard which certainly should be avoided if possible. Consequently, the usual treatment of choice at Presbyterian Hospital has been the installation of fine wire into the sac. I am speaking now of the saccular type, such as were presented today. Our experience with this method has been extremely good, the mortality being essentially zero. The pulsatile character of the sac, pain related to the bone erosion, and the actual size of the aneurysm has definitely decreased following application of between two and five hundred feet of wire. In some cases several applications of wire may be needed.

Dr. Blakemore himself prefers an apparatus which converts alternating current to direct current to permit electrothermal coagulation in the sac. He instills a specially insulated, flexible fine wire into the sac, which he heats at 80° C. for about ten seconds. This causes a coagulum to form on the wire mesh and perhaps produces a much quicker inactivation of the sac. I have not used this particular apparatus, but have relied mainly on 32-gauge steel wire. My results in a small series of cases have been very satisfactory also. Recently, I have been looking for cases such as were reported here in which we might be able to resect the sac and use a preserved homograft. I feel that any other method than actual restoration of a normal linear channel of blood flow is somewhat short of what we would like to achieve.

DR. OSLER ABBOTT, Atlanta, Ga.—I should like to speak on three points. Our feeling with regard to aneurysm has been that whenever possible they should be resected. When they cannot be resected then we use a combination of Cellophane wrapping and wire, except in the ascending aorta, and the arch of the aorta, because of the frequency with which wiring has produced fatal cerebral involvement phenomena. The second point I would like to bring out is the symptomatology due to stimulation of the adventitia of the aorta in the traumatic

cases. These patients will frequently have burning pain, particularly during the night, quite similar to that of myocardial infarction. The third point I would like to mention is to try to clarify rather than confuse the situation with regard to Cellophane. The DuPont Company notified us quite a while ago, and I know that Dr. Poppe had considerable correspondence with them, to the effect that they wish to be of all help possible to the medical profession, but are not a pharmaceutical house; they have now discontinued making, or stopped supplying as such, reactive and nonreactive Cellophane. What we have done is to follow the work of Dr. Hufnagel and make our Cellophane nonreactive by soaking it long enough in alcohol. Then we make a supersaturated solution of diacetyl phosphate powder in toluol. We then paint this material under aseptic precautions on the Cellophane that we want to make reactive, then put it in zephiran for twenty minutes. There is no question that the reactivity is far superior to any that we have used before.

DR. ROLLIN A. DANIEL, Nashville, Tenn.—We have quite recently had the opportunity to operate on a Negro woman 67 years old, with a large aneurysm of the ascending aorta, with erosion of the sternum and marked tracheal obstruction. She had been unable to lie in bed for several weeks before the time she came to the hospital.

(Slide.) We excised the aneurysm at its base. The patient expired four hours after she was returned to bed, of cardiac arrest. Resuscitation was possible, but another arrest occurred about an hour later, and another, and she expired. There are a few points, however, which I think may be worth mentioning. This slide shows an area where the aneurysm was dissected and the roughened area. This was an arteriosclerotic aneurysm; there was much calcium in the wall of the aorta. We dissected gradually and found it had a pedicle about two inches in diameter, considerably smaller in diameter than was at first realized.

(Slide.) This depicts the suture line after excision of the aneurysm. The fact that she died leaves unanswered any question as to the fate of this suture line. Two other points which I think may be helpful, however, are first, the exposure, which was very good, obtained by transecting the sternum and crossing the anterior intercostal spaces, and then dividing the cartilages on each side. After they were divided the sternum protruded far forward. Second, just as the clamp was placed across the pedicle, the aneurysm was opened at its apex and clots and bright blood in small amounts from the aorta were evacuated, at the same time the clamp was tightened. I think that cutting through or fracture of the base of the aneurysm would have been more likely had the sac not been opened widely before the base of the aneurysm was clamped.

DR. MC COOEY (Closing).—I wish to thank Dr. Cooley, Dr. Deterling, Dr. Abbott, and Dr. Daniel for their excellent contributions to this presentation. Our conclusion is that it is obvious further observation is necessary, and it is hoped that the recording of this small series will stimulate such a study.

HEALING OF EXTENSIVE CARDIAC WOUNDS

COLIN G. THOMAS, JR., M.D. (BY INVITATION), CHAPEL HILL, N. C., AND SIDNEY E. ZIFFREN, M.D. (BY INVITATION), IOWA CITY, IOWA

THIS study was undertaken because it was evident that continued progress in surgery of the heart would depend upon greater knowledge of the consequences of cardiotomy. Little information was available regarding the formation of mural thrombi and subsequent embolization following incisional wounds; neither was information available regarding dehiscence of the wound, aneurysm, or rupture of the site. Accordingly, the investigation was designed to study the healing of the myocardium following extensive incisional and excisional wounds of the anterior wall of the left ventricle.

From clinical practice it is known that cardiotomy is feasible, and considerable experience has accumulated in surgery directed toward valvular diseases of the heart, removal of foreign bodies, and repair of stab wounds. In these instances the defects of the ventricular wall have been relatively small, and healing has usually been without complication. However,[14] an aneurysmal dilatation has been noted ten months following cardiotomy for aortic valvular disease, and in another instance[10] an embolus to the brain followed the repair of a stab wound. No long-term analyses have been reported regarding the course and end results of myocardial repair.

Cardiac muscle is a peculiar type of striated muscle and exhibits only slight capacity for regeneration.[11] Consequently, union is a function of the development of a fibrous scar strong enough to bridge the defect without yielding to intermittent intracardiac pressure.

From the general principles of wound healing, the course of myocardial repair may be fairly well anticipated.[7] An initial "lag" period of several days would be followed by a second phase of increasing strength due to the rapid proliferation and slower maturation of the fibroblast. In structures with a high tensile strength, the third phase of increasing strength coincident with the maturation and increase in amount of collagen extends over weeks rather than days. Ultimately, the tensile strength of a wound is almost entirely a function of the number of fibroblasts, their maturation, and the adequacy of collagen formation. Scar tissue, however, is seldom as resistant to tension as is normal tissue.[5, 13] Thus, if tension is present in any degree, the cicatrix may prove to be a vulnerable point in that area subjected to such pressure or tension. The heart muscle is unique in that it is constantly undergoing contraction and relaxation, and yet is at all times under tension.

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Read at the Thirty-second Annual Meeting of The American Association for Thoracic Surgery at Dallas, Texas, May 8-10, 1952.

On a theoretical basis, with the knowledge of wound healing as described and the changes that may result in a scar from prolonged tension, some attenuation of cicatrix joining cardiac muscle can be anticipated. Furthermore, the physical forces are such that under certain circumstances the resulting scar would not only become attenuated, but possibly rupture or develop an aneurysmal defect. A somewhat analogous situation exists following coronary occlusion and subsequent myocardial infarction in which both rupture and aneurysm are known to occur. The development of such an aneursym closely follows the occurrence of myocardial infarction, appearing within a week to several months after the acute episode.[1]

Relatively few experimental studies have been directed toward this problem. Those by Elsberg[3] in 1899 concerned the healing of heart wounds in rabbits, and disclosed the development of a scar that did not interfere with cardiac function. His observations extended over a four-week period, and in only one instance was the scar noted to be "thin and bulging." More recently, Carter observed broadening and thinning of the cardiac wound following excision of portions of ventricles.[2] These observations extended over a period of six months.

METHODS

Adult mongrel dogs weighing between 10 and 25 kilograms were utilized as the experimental animal. Employing intravenous pentobarbital sodium for anesthesia in conjunction with an intratracheal airway, thoracotomy was performed through the left fifth interspace. Ventilation was maintained manually while the chest was open. After dividing the pericardium parallel and medial to the left phrenic nerve, exposure of the anterior surfaces of the right and left ventricles was obtained. The heart was bathed periodically with 2 per cent procaine to reduce irritability[6] and to maintain moist surfaces. One suture was placed through the apex of the heart to facilitate control. Two groups of experiments were then carried out:

1. An area measuring approximately three by four centimeters, including the entire thickness of the left ventricular wall, was excised. This area was delineated by ligating an inferior twig of the descending branch of the left coronary artery and accompanying vein. The region of subsequent ischemia measured approximately two by three centimeters on the anterior surface of the left ventricle. This area plus the surrounding three to five millimeters of cardiac muscle was then excised, attempting to divide the myocardium at right angles to its epicardial surface. The ligation of these small vessels usually does not produce an infarct,[12, 15] but serves merely to outline that area in which circulation might be temporarily impaired by interruption of these vessels at the time of excision. Incisions in this area are inferior to the papillary muscles and do not encroach upon the interventricular conduction mechanism. The resulting defect in the ventricular wall was closed by interrupted through-and-through sutures of No. 000 black silk. These sutures were placed approximately three-fourths to one centimeter apart and from one to one and one-half centimeters from the wound margin, passing through the epicardium, myocardium, and endocardium. The average length of the closed incision on the epicardial surface was between three and four centimeters, requiring five to six sutures for closure. Fifteen dogs were available for periodic examination during the course of wound healing, with observations made over a period of forty-six months.

2. A linear incision was made in the left ventricular wall parallel to the interventricular septum beyond the gross arborizations of the rami of the anterior descending branch of the left coronary artery. The incision was approximately four centimeters in

length. Twelve dogs were observed over a period of eleven months. In two additional animals a two-centimeter incision in the same location was carried out. Closure was effected as described in Group 1.

Since the techniques employed for limiting blood loss are not pertinent to this discussion, they will be described only briefly. Three methods were utilized. (1) Excision of the ventricular wall was performed with the blood loss being proportionate to the time required for wound closure. (2) Underlying mattress sutures were placed prior to incision of the myocardium and subsequently removed after closure of the cardiac defect. (3) In the majority of animals the superior and inferior venae cavae were clamped, occluding the return flow of blood to the heart, except that through the azygos vein and coronary sinus, This last method was found to be the most expedient as far as diminishing blood loss was concerned, and also decreased manipulation of and trauma to the heart. Wound healing followed the same general pattern regardless of the technique employed.

In the pilot experiments, serial electrocardiograms were procured during all phases of the procedure as well as early and late in the postoperative period. The animals were sacrificed at periodic intervals under pentobarbital sodium anesthesia. In each instance the heart was observed directly for evidence of cardiac aneurysm.

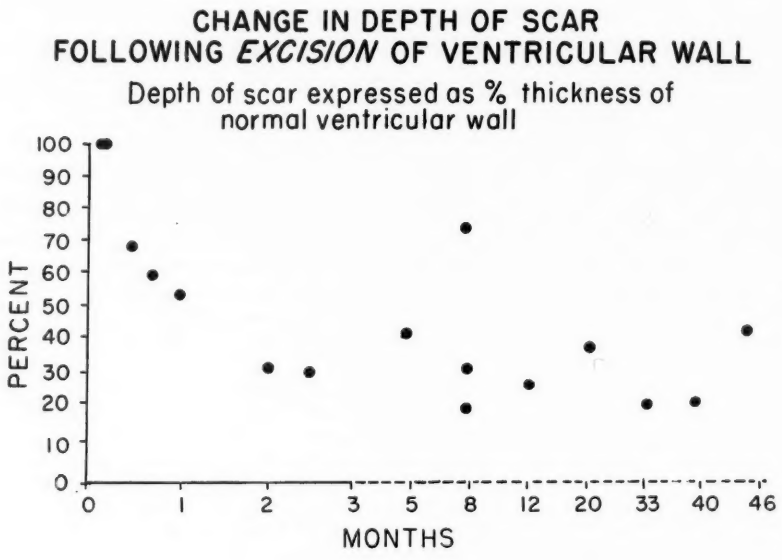

Fig. 1.

RESULTS

Group 1.—With excision of a portion of the ventricular wall healing was characterized by the early production of a narrow scar measuring the entire thickness of the apposed surfaces. This depth of scar was maintained for approximately one to two weeks, and then rapidly decreased in thickness during the ensuing two weeks so that at the end of one month the cicatrix joining cardiac muscle measured only 50 per cent of the thickness of the adjacent normal ventricular wall.* With increasing intervals of time there usually developed

*All measurements were taken from the midportion of the scar, which was usually thinnest, with graduation toward extremities.

attentuation until the scar measured 30 per cent of the ventricular wall (Fig. 1). In some instances this developed as early as two months, whereas in others a relatively thick scar was maintained until the time of sacrifice at eight months. The greatest attenuation was observed in those animals sacrificed at thirty-three and forty months (Fig. 2).

Concomitant with early healing, there also occurred increase in breadth of the scar so that in its midportion it usually measured between nine and eleven millimeters. These changes were observed as early as one week, and seemed to bear no direct relationship to the depth of the scar or the elapsed time (Fig. 3).

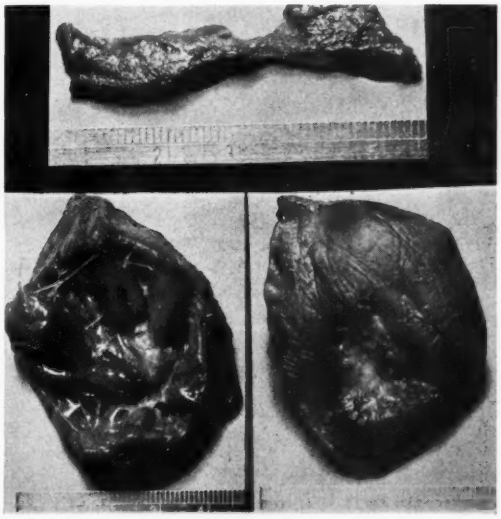

Fig. 2.—Endocardial, epicardial, and cross-sectional views of heart thirty-three months following excision of 2 by 3 cm. area of left ventricular wall.

Group 2.—With linear incision of the ventricular wall the course of healing was essentially as observed in Group 1. Differences in degree were noted, however; viz., attenuation of the cicatrix was present but was less pronounced, and in only one instance was it less than 50 per cent of the thickness of the adjacent ventricular wall (Fig. 4). There was also more variation in the maximum breadth of the scar, which varied from two to eleven millimeters. Again there was no correlation with elapsed time or depth of scar. In the two dogs in which two-centimeter incisions were made in the same location, very little tendency toward attenuation was observed over a period of four and six months (Fig. 4).

In all dogs the following features were observed to occur without regard to the particular procedure carried out.

1. *Histologic changes.*—Microscopic examination disclosed an initial death of that cardiac muscle made ischemic by wound closure. This zone of necrosis

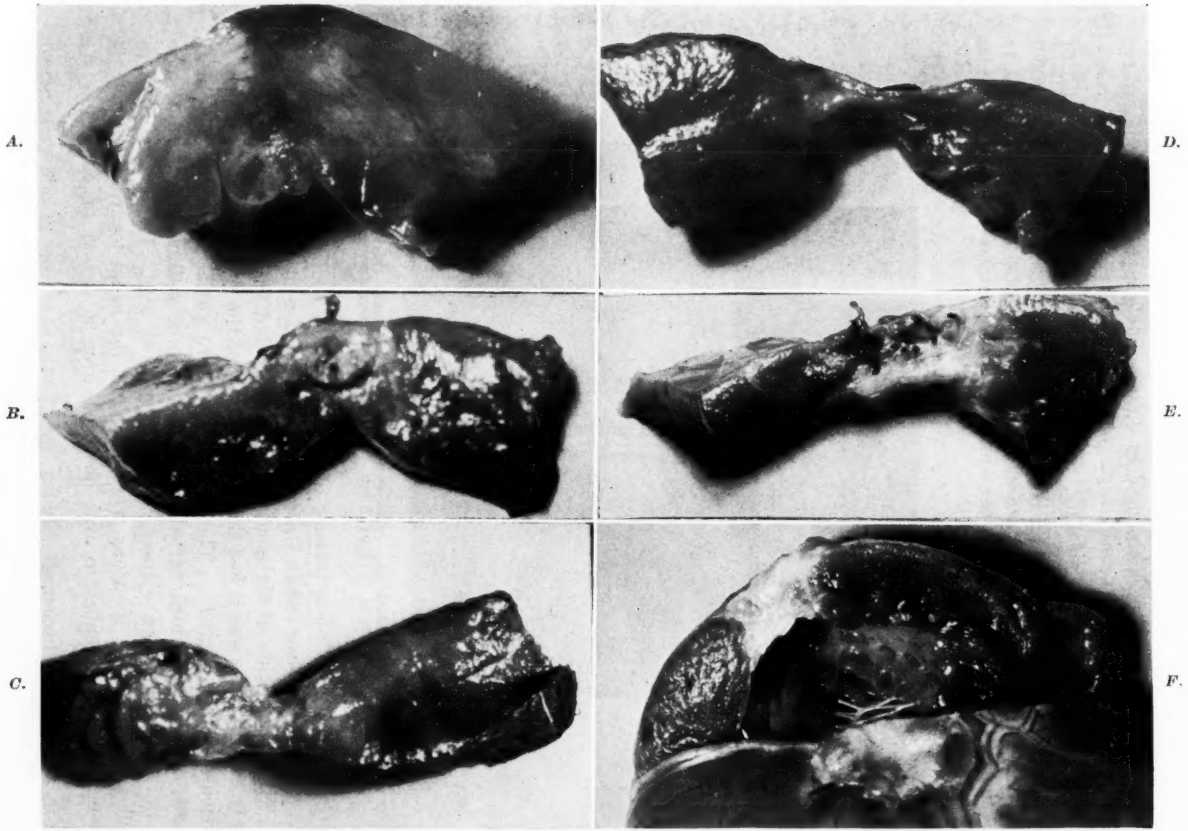

Fig. 3.—Cross-sectional view through midportion of scar at indicated interval from time of cardiotomy. Note variation in breadth and depth of scar. *A*, One week; *B*, two weeks; *C*, one month; *D*, two months; *E*, three months; *F*, twenty months.

was variable in width, and in a few instances involved the entire portion of the myocardium imprisoned by suture material. The necrotic muscle was rapidly invaded and replaced by granulation tissue apparently arising from adjacent viable myocardium (Fig. 5). Complete replacement was usually present between two and three weeks. The more mature scar was characterized by an abrupt transition from relatively normal myocardium to dense, at times almost hyalin, cicatrix. The production of cartilage and bone was observed in one instance. Considerable reaction was present about the suture material, and, as was noted grossly, the scar usually extended two to five millimeters beyond the sutures.

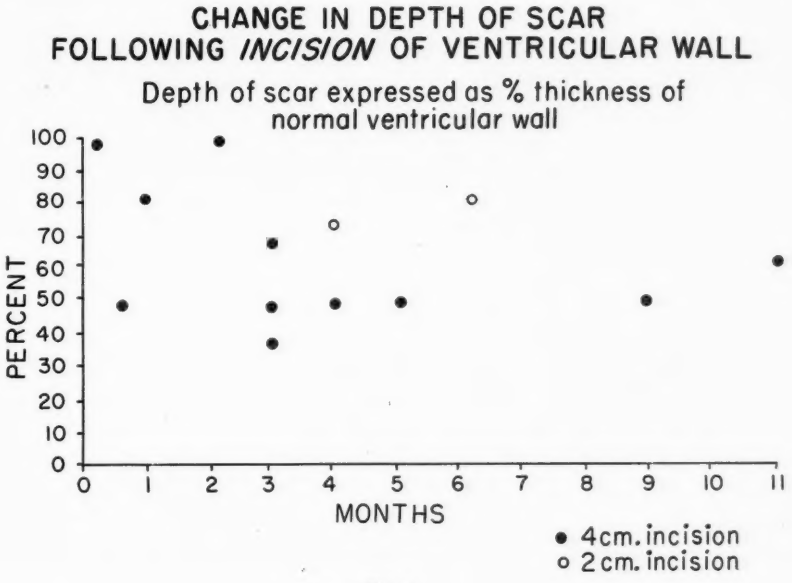

Fig. 4.

2. *Endocardial healing.*—Within one week both the suture material and denuded endocardial surface were covered with a thin layer of fibrin. Rapid surfacing with a mesothelial or endothelial-like lining occurred which was usually complete at two weeks. Thereafter the endocardial scar remained smooth, with the suture material well embedded within the scar.

A limited number of observations over a period of eleven months were made on healing following placement of sutures without engagement of the endocardium. They would suggest that attenuation is the same or somewhat less than when through-and-through sutures are placed. Furthermore, broadening of scar was less conspicuous on the endocardial surface. These findings may be attributed to the failure of incorporation of the endocardium resulting in less tissue necrosis and to the foreign body reaction being limited to the myocardium.

3. *Thrombus formation and embolism.*—There was no evidence of embolism in any of the dogs observed. In seventeen hearts examined between one and ten days postoperatively, only two instances of mural thrombus occurred. In one of these, a relatively large area of necrosis was present at the suture line.

4. *Epicardial healing.*—The epicardial scar was greater in breadth than that on the endocardial surface, and was adherent to the pericardium. In a few animals the suture material seemed to be extruded toward the epicardial surface (Fig. 3, *E*, three months).

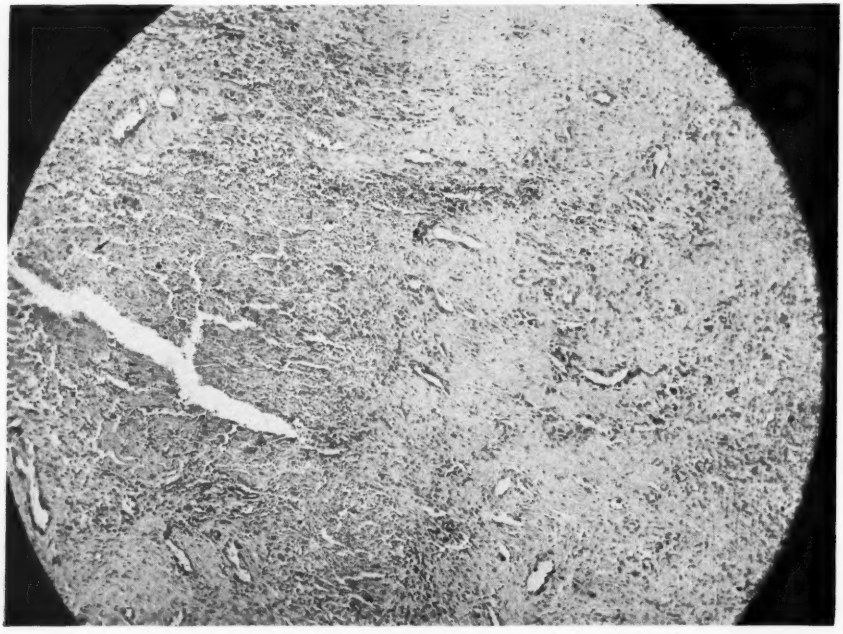

Fig. 5.—Healing at two weeks. Note replacement of dead muscle by granulation tissue.

5. *Wound dehiscence.*—Rupture of the myocardium at the site of suture occurred in three of twenty-seven dogs surviving partial excision of the ventricular wall, and in three of eighteen dogs surviving linear incision for an over-all incidence of 13.3 per cent. This complication occurred early in the course of the experiments, and with greater experience was practically eliminated. In every instance in which rupture occurred there was necrosis of a portion of the myocardium contained within the suture line. Dehiscence occurred within one to seven days postoperatively.

6. In no instance did death occur from bleeding at the site of the suture line or from cardiac tamponade.

7. *Aneurysmal defects* did not develop, although in three animals (Figs. 1 and 2) the scars measured between one and two millimeters at the thinnest point. It is conceivable that if these animals had been permitted to survive a longer period of time aneurysmal dilatation might have occurred.

8. *Cardiac failure* was not observed.

9. *The electrocardiographic findings* were those of mild changes in the T waves similar to those observed by Fowler and associates.[4]

10. *Adhesive pericarditis.*—A significant number of animals were noted to have an adherent pericardium which snugly fit the epicardial surface. This was particularly adherent at the site of myocardial incision and damaged epicardium. Although in many animals the pericardium seemed to tightly encompass the heart, there was no evident increase in venous pressure, ascites, or peripheral edema. In those hearts with a "tight" pericardium, the heart was seen to bulge through the pericardium upon its incision. Although cartilage and bone formation were observed in myocardial scars, none was noted involving or arising in adherent pericardium. No relationship was observed between time and adherence of pericardium and essentially none between the type of experimental procedure and the degree of adherence.

DISCUSSION

These findings indicate that, despite a relatively large cardiac wound, repair is carried out in a manner similar to that observed in other tissues in which regenerative capacity is nil. Thus, the defect created is effectively bridged for functional purposes. Although on a theoretical basis sufficient attenuation of a large wound to produce rupture or an aneurysm would seem a real possibility, it was not observed experimentally. It is apparent that the degree of attenuation is dependent upon several factors. The relatively greater depth of scar observed after linear incision as compared to partial excision can probably be attributed to a nicer coaptation of wound margins so that the entire ventricular wall is in apposition. It is unlikely that any theoretical changes in interventricular tension due to decrease in size of ventricular capacity would account for such differences. There was less attenuation in relatively short, two-centimeter, incisions than in those twice this length. Although in general the degree of attenuation remained fairly constant regardless of the thickness of the ventricular wall, those regions near the apex measured the thinnest in terms of millimeters, and it is in these regions that an aneurysmal dilatation would seem most likely to occur. Another factor must be the amount of muscle made ischemic by an encircling suture. If great enough the course of repair would be more analogous to that of a healing myocardial infaret.

Although it has been recommended that sutures be placed so they do not penetrate the endocardium,[3, 10] this requires a nicety of placement that is seldom realized under the present circumstances. Furthermore, the sutures within the ventricular lumen are soon covered with a thin layer of fibrin and are no more dangerous as a source of emboli than the denuded cardiac muscle, although theoretically, with perfect wound coaptation, the endocardial surface would be intact. As has been the experience with intimal sutures within the aorta, the presence of a rapid blood flow seems to minimize the chance of a large thrombus being formed and subsequent embolization.

A limited number of observations suggest that additional cardiac load produced by an arteriovenous fistula, sufficient to result in mild cardiac hyper-

trophy, does not materially affect the course of healing as described. Increase in body weight—heart weight ratio was used as a criterion of hypertrophy.[8, 9]

Wound dehiscence seems primarily to depend upon the amount of necrosis of cardiac muscle caused by the wound closure. With experience in the placement of sutures and the attainment of appropriate degrees of tension, this complication should be obviated.

SUMMARY

1. Repair of large cardiac wounds in the dog was characterized by production of a dense scar uniting the wound margins without apparently impairing cardiac function.

2. Attenuation of this scar occurred so that at one month it measured 50 per cent of the thickness of the adjacent normal ventricular wall and usually continued until the scar measured 30 per cent of this thickness. These changes occurred over a period of several months.

3. There were considerable variations in the breadth of the scar.

4. No evidence of aneurysm was observed in the scars under normal and under increased cardiac load.

5. Embolism was not observed following any of the procedures.

6. The strongest scar was obtained with the shortest incision through the thickest part of the myocardium in conjunction with maximum wound apposition by sutures causing minimal ischemia.

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HEMOPERICARDIUM AND CONSTRICTIVE PERICARDITIS

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THE development of the majority of cases of constrictive pericarditis is not well understood. Tuberculosis has been implicated in from 10 to 28 per cent of various collected series such as those reported by Beck[1] and Chambliss.[2] The remainder have been ascribed to acute pyogenic infection, rheumatic fever, polyserositis, or unknown causes. The pathologic findings of those in the latter categories usually show nonspecific fibrosis with or without calcification. Frequently there is nothing to suggest tuberculosis or a specific etiologic agent. It is this group of patients we are concerned with in this publication.

The occurrence and subsequent operation of a patient with chronic hemopericardium and early constrictive pericarditis which developed following nonpenetrating minimal precordial trauma was recently observed by the authors. Relatively minor precordial trauma, followed by development of a chronic hemopericardium, was clearly established in the development of this case. The postulation of such a sequence of events operating in patients with nonspecific constrictive pericarditis is worthy of further study. The etiologic relationship between pericardial hemorrhage produced by trauma and late chronic constrictive pericarditis has perhaps been overlooked. Chronic pericardial effusion and pericardial hemorrhage may remain relatively asymptomatic for long periods of time until definite symptoms of constrictive pericarditis become apparent. This latent period of varied length has been mentioned in the few reported cases.

REVIEW OF LITERATURE

Interest in the etiology and development of constrictive pericarditis was first recorded by Beck in 1929[3] and 1930,[4] who investigated the results of Dakin's solution placed within the pericardial sac. At this time the possible end results by using this solution for irrigation in cases of purulent pericarditis were under investigation using dogs as experimental animals. A hemorrhagic pericarditis was produced by this solution which was followed by late constrictive pericarditis.

The possible role of hemorrhage into the pericardial sac and its relation to constrictive pericarditis was first suggested by Daniel and Puder[5] in 1932. Autopsy findings in their case consisted of precipitated cholesterol within the pericardium. Hemorrhage, followed by precipitation of blood lipids and subsequent pericarditis, was offered to explain the pathogenesis. White[6] mentions the possible role of traumatic hemopericardium in the etiology of

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Read at the Thirty-second Annual Meeting of The American Association for Thoracic Surgery at Dallas, Texas, May 8-10, 1952.

adhesive pericarditis in the 1937 edition of his textbook. Extensive constrictive pericarditis was found at autopsy by Glenn[7] in a patient who had suffered a crushing injury to the chest three years ante mortem. This author felt that traumatic hemopericardium was responsible in his case. Hemosiderin and lipids were found microscopically in a case of hemorrhagic pericarditis by Voldet.[8] Recurrent hemorrhage was believed the etiologic factor in this presentation, and the author implicated either trauma or myocardial infarction as the source of bleeding. Pericardiectomy was performed by Dejou[9] in a 19-year-old soldier for hemopericardium which followed nonpenetrating chest trauma. Syphilis was implicated in one of four cases of chronic hemorrhagic pericarditis by Froment and associates.[10] One of three patients with chronic constrictive pericarditis reported by Barker and Johnston[11] required pericardiectomy three years following trauma to the chest cage. Ada and associates[12] report a somewhat similar situation, and present the microscopic findings. The patient had experienced three episodes of nonpenetrating chest trauma during the two years prior to pericardiectomy.

The most recently reported case was that of Overholt and associates.[13] Bilateral fibrothoraces accompanied the chronic constrictive pericarditis. Decortication of all three sites resulted in improvement. Nonpenetrating trauma preceded surgical treatment by five years, and the symptoms resembling Pick's disease were well developed at that time. Sterile hemopericardium and hemothorax were thought to be the etiologic factors. This is the first recorded case studied pre- and postoperatively by cardiac catheterization and ventilatory function studies.

The aspiration treatment of pericardial tamponade following penetrating cardiac wounds has been reported by Elkin and Campbell[14] and Ravitch.[15] Development of the process under discussion in this situation would seem a real possibility. The question has been raised whether blood left within the pericardial sac would not eventually lead to the development of constrictive pericarditis. We did not observe blood to be clotted within the pericardial sac of the case which is presented, but that this may occur has been mentioned by Maguire and Gage.[18] Well-developed chronic constrictive pericarditis was found in one of Maguire's patients who had been treated for a penetrating cardiac wound by aspiration six months previously.

Unfortunately, the type of patient most likely to incur this injury is not often available for follow-up study. Chronic constrictive pericarditis has not been observed by either Elkin[16] or Ravitch[17] in their cases treated by pericardial aspiration. That this train of events may occur more frequently than the literature indicates seems entirely possible.

Two cases of cholesterol pericarditis are to be found in the English literature. The most recent by Ada and associates[19] was of unknown cause. A chronic constrictive pericarditis was found. The granulation tissue and scar contained cholesterol crystals. Unrecorded and unremembered precordial trauma producing hemopericardium must be considered as a possible etiologic agent.

In a collected series of 261 cases of nonpenetrating injury to the chest, Warburg[20] found evidence of pericardial hemorrhage in 23 per cent.

Kerley[21] feels that cases of calcific pericarditis may well be due to a traumatic hemopericardium rather than to specific infections such as tuberculosis.

CASE REPORT

K. D., a 35-year-old white truck driver, entered the University Hospitals on Jan. 4, 1951. Admission was prompted because of bleeding from a left bronchopleurocutaneous fistula which had persisted after drainage of a lung abscess at the age of 4 years. He was a well-developed and well-nourished man in no acute distress. He was afebrile, and the blood pressure was 120/85. A large bronchopleurocutaneous fistula overlying the left fifth rib was present. The remainder of the physical examination was essentially normal.

Bronchograms revealed bronchiectasis involving the lingular segment of the left upper lobe and the bronchial fistula leading into this pulmonary segment. On Jan. 10, 1951, a left upper lobectomy was performed. Convalescence was uneventful, and the patient was discharged in good condition on Jan. 21, 1951. An electrocardiogram was normal. Roentgenograms of the chest at the time of discharge showed a normal heart shadow and a well-expanded left lower lobe.

The patient was readmitted on July 25, 1951. He had gained twenty-one pounds, and had resumed work. No unusual symptoms were noted, but upon more thorough questioning it was discovered that he had noticed some shortness of breath and easy fatigue during the past few weeks.

A routine roentgenogram of the chest revealed a huge pericardial shadow. This was an entirely unsuspected finding, and it was only following further questioning that he recalled being struck by a baseball over the precordium six weeks prior to this admission. On July 27, 1951, the pericardial sac was tapped and 20 c.c. of old, dark blood was removed. Venous pressure readings were 170 mm. of saline. On July 30, 1951, the pericardial tap was repeated, and at the same time cardiac catheterization studies were carried out in the cardio-

TABLE I. COMPARATIVE STUDIES OF PERICARDIAL FLUID AND PERIPHERAL VENOUS BLOOD

	PERICARDIAL FLUID			PERIPHERAL VENOUS BLOOD		
Plasma proteins	T 660	A 4.32	G 2.28	T 7.35	A 4.63	G 2.72
Chlorides	680 mg. per cent			675 mg. per cent		
Cholesterol	66 mg. per cent			108 mg. per cent		
Cholesterol esters	36 mg. per cent					
Blood urea nitrogen	18 mg. per cent			18 mg. per cent		
Creatinine	2.2 mg. per cent			1.6 mg. per cent		
CO_2 combining power	47 c.c.			54 c.c.		
Oxygen content	2.08 vol. per cent			16.36 vol. per cent		
Van den Bergh	1.5 mg. per cent—1 min. 15.6 mg. per cent—30 min.					
Hemoglobin with related heme pigments (normal 20 mg. per cent)	264 mg. per cent					
Hemoglobin	8.1 Gm.			15.3 Gm.		
Hematocrit	22 per cent			52 per cent		
Erythrocyte count	2.62 million			5.23 million		
Leukocyte count	5,500			7,800		
Differential count	segs 6 per cent lymphs 93 per cent monos 1 per cent			segs 71 per cent lymphs 26 per cent monos 2 per cent eosinophils 1 per cent		

vascular laboratory.* Three-hundred eighty cubic centimeters of dark blood were withdrawn, and two hundred fifty cubic centimeters of air injected. Withdrawal of the fluid caused simultaneous decline of elevated intrapericardial and right intra-atrial pressures toward normal. The fixed cardiac output revealed a significant degree of tamponade or constriction. Comparative studies of pericardial fluid and peripheral venous blood are shown in Table I.

On Aug. 3, 1951, a partial pericardiectomy was performed. Most of the pericardium overlying the left ventricle and right ventricle was excised. About 500 c.c. of old, nonclotted blood were removed from the pericardial space. The pericardium was noted to be four to six times its normal thickness. There was extensive organizing granulation tissue over the epicardium and pericardium. No significant bleeding points were found within the pericardium at operation. An electrocardiogram showed a decrease in the QRS and T waves. His postoperative course was uneventful, and he was discharged on Aug. 12, 1951.

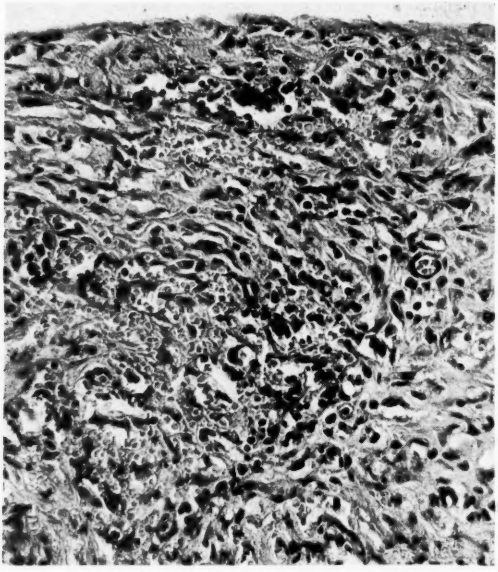

Fig. 1.—Photomicrograph of excised pericardium showing organizing granulation tissue of reported patient with chronic hemopericardium.

Microscopically the sections show extensive nonspecific granulation tissue and scar. The strikingly thickened pericardium showed scarring in various forms of organization from fibrin most superficially to relatively avascular laminated collagen in the deeper layers. There was chronic inflammation and foreign-body giant-cell reaction present. Considerable vascularity was seen throughout, most apparent in the areas of organizing granulation tissue. Many phagocytes containing blood pigment were noted (see Fig. 1). The pericardial blood was inoculated into a guinea pig and reported as negative for tuberculosis. A bacterial culture proved it to be sterile.

The patient was readmitted on Aug. 24, 1951. His vital capacity at this time was 2.8 liters. He had been working and felt much better than he had prior to the last admission. The venous pressure was 85 mm. of saline and the circulation time, arm to tongue, was 18 seconds using Decholin. A roentgenogram of the chest revealed a heart of normal size. A roentgenkymogram showed normal cardiac movements. An electrocardiogram showed only inverted T waves. Cardiac catheterization was performed and revealed essentially normal resting values (see Table II). He was discharged on Aug. 28, 1951.

*These findings will be reported in detail by Ames and associates, *American Journal of Medicine* (in press).

The last admission occurred on Feb. 26, 1952. A roentgenogram of the chest revealed again a normal cardiac silhouette (see Fig. 2). Resting values during cardiac catheterization at this time were essentially normal. He did, however, have a fixed cardiac output under exercise. This was interpreted as showing some evidence of limited cardiac expansion. The

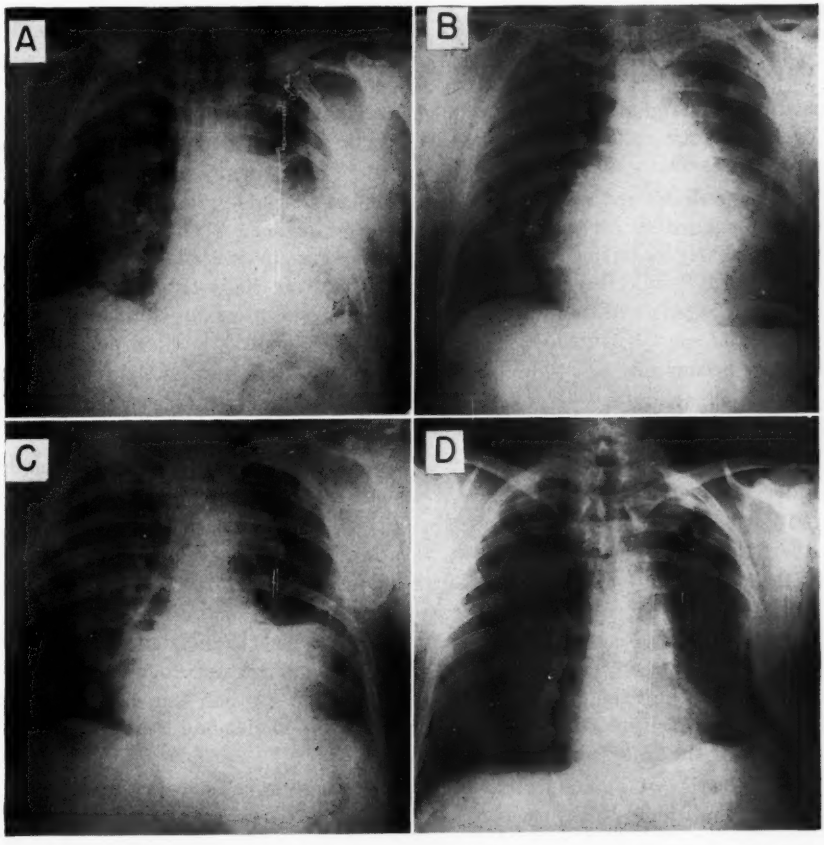

Fig. 2.—Roentgenograms of chest of patient with chronic hemopericardium. *A*, Jan. 21, 1951, normal configuration of heart following left upper lobectomy. *B*, July 23, 1951, massive pericardial effusion at time of first readmission. *C*, July 30, 1951, after withdrawal of 380 c.c. of pericardial fluid and injection of air. *D*, Feb. 26, 1952, normal cardiac configuration after pericardiectomy at time of final admission.

patient is being observed at the present time for the development of further symptoms. It is possible that he will require excision of the thickened epicardium which was a poorly defined layer at the time of the pericardiectomy.

EXPERIMENTAL DATA

The poor absorptive powers of the rabbit pericardium were studied by Drinker[22] and human pericardium by Stewart.[23] They found that electrolytes but not colloid particles were taken up by the pericardium. The rabbit peri-

TABLE II. CARDIAC CATHETERIZATION DATA

PRESSURES (MM. HG.)	NORMAL	PREOPERATIVE	3 WEEKS POSTOPERATIVE
Right atrium	8/0	20/15	10/2
Right ventricle	30/0	32/12	21/0
Pulmonary artery	30/15	31/16	26/15
Pulmonary capillary	6	12	5
Cardiac output at rest (liters per minute)	6.0	6.4	6.75

cardium was found to contain very few lymphatic channels which accounted for the scanty colloid removal. Electrolytic solutions were easily removed through vascular channels.

The well-defined sequence of events, namely, hemopericardium produced by nonpenetrating precordial trauma, followed in seven weeks by the development of early constrictive pericarditis in the case presented, prompted us to make the following investigation. An attempt was made to produce chronic constrictive pericarditis by injecting the lipid fraction of dog's blood into the pericardial sac. Upon suggestion by Dr. N. A. Womack the lipid portion was utilized because it was thought that it might be the most likely fraction to produce inflammatory response. Another series of animals was maintained simultaneously by injecting autogenous blood into the pericardial sac.

Fourteen mongrel kennel dogs were utilized. The injections were made under intravenous Nembutal anesthesia using controlled endotracheal oxygen ventilation. The animals varied in size between nine and fourteen kilograms. A left thoracotomy was carried out, and the injections made through a needle in the pericardial sac. The needle wound was ligated to prevent leakage of the injected material. The series of animals in which blood was used served as their own donors, the blood being aspirated from the auricle or ventricle and injected directly into the pericardial sac. The largest dogs received 100 c.c. of blood, and the smallest received 50 c.c. More than this amount of injected blood frequently precipitated acute tamponade, and required partial removal of the injected material.

The series of animals receiving lipid extract were operated upon under similar conditions. They received the lipid fraction of 100 ml. of dog blood in 25 ml. of phosphate buffer suspension having a pH of 7. This suspension was injected in a like manner. The lipid fraction was extracted from pooled dog's blood by the following method. The blood was collected in 500 ml. of extracting fluid containing 1:1:1 ratio of acetone, alcohol, and ether. The resultant suspension was filtered through a Büchner funnel and washed with several portions of extracting fluid. The filtrates were pooled and evaporated. The lipid fraction was prepared for injection by placing 600 mg. of the evaporated material in 25 ml. of phosphate buffer, emulsifying it in a Waring blender. The material was then sterilized in rubber-stoppered bottles at 15 lb. pressure for fifteen minutes. Plasma determinations on whole donor dog blood showed cholesterol 130 mg. per cent and proteins 6 to 8 Gm. An analysis of the lipid fraction extracted from pooled whole dog's blood yielded the

following: 600 mg. lipid fraction contained cholesterol (Liebermann-Burchard method) 52 mg. or 8.7 per cent, phospholipids (Gibson's method) 490 mg. or 81.7 per cent, and the remainder, 58 mg. or 9.6 per cent of other lipid material.

Two dogs each of the blood and lipid series were sacrificed at intervals of one, three, and six months. Two dogs injected with a suspension of crystalline cholesterol in saline were sacrificed at six and ten weeks each.

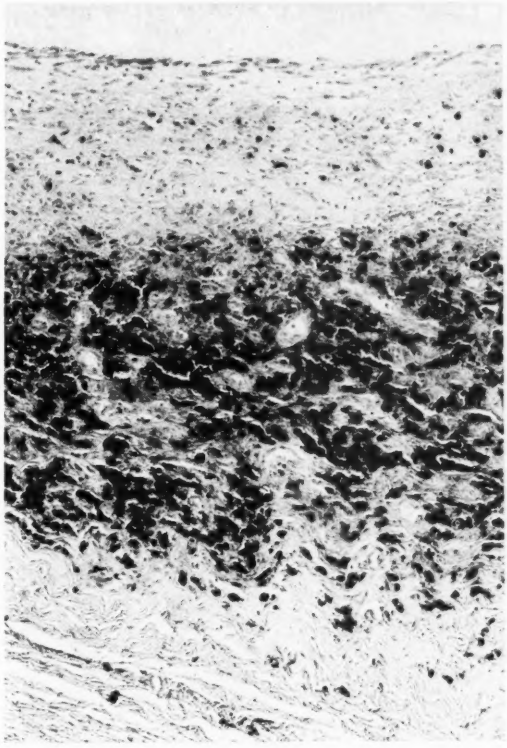

Fig. 3.—Photomicrograph of epicardium of a dog sacrificed one month after injection of 100 c.c. of autogenous blood. Scarring, inflammatory response and pigment-laden phagocytes are seen (iron stain).

EXPERIMENTAL RESULTS

All animals of both series showed changes in the pericardium and epicardium. The amount of scar tissue response varied from rather minimal changes in some of the dogs with hemopericardium to far-advanced hemorrhagic constrictive pericarditis in one dog of the lipid series. The pericardial tissue of all animals was examined microscopically using hematoxylin-eosin, iron, and special fat stains. None of the dogs who had autogenous blood injected into the pericardial sac developed advanced changes of constrictive

pericarditis. These animals showed patchy pericardial and epicardial scarring without formation of a constrictive envelope. Adhesions between the pericardial and epicardial layers were not a prominent feature. None of the

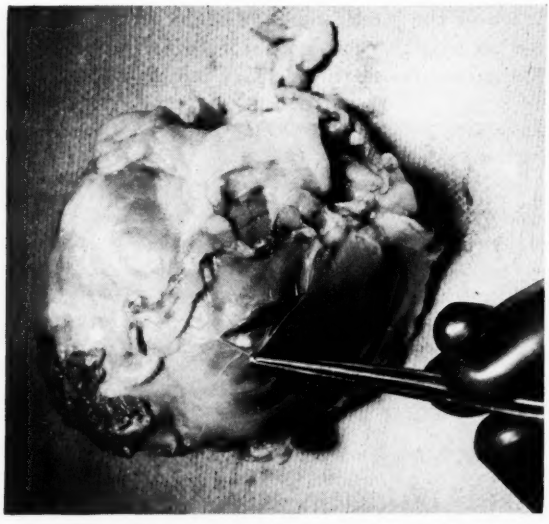

Fig. 4.—Photograph showing heart of a dog injected with blood lipid fraction sacrificed at three months. Adhesive pericarditis is demonstrated.

Fig. 5.—Photograph showing the dog heart seven weeks after injection of blood lipid fraction. Extensive hemorrhagic constrictive pericarditis is shown.

injected blood was found in any of the dogs at the time of autopsy, and none of the pericardial findings were more marked in the dogs sacrificed at longer intervals.

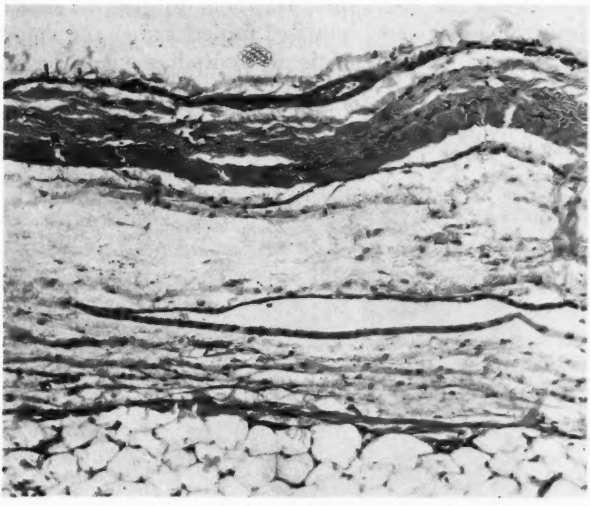

Fig. 6.—Photomicrograph showing adhesive pericarditis in a dog injected with lipid suspension three months before sacrifice.

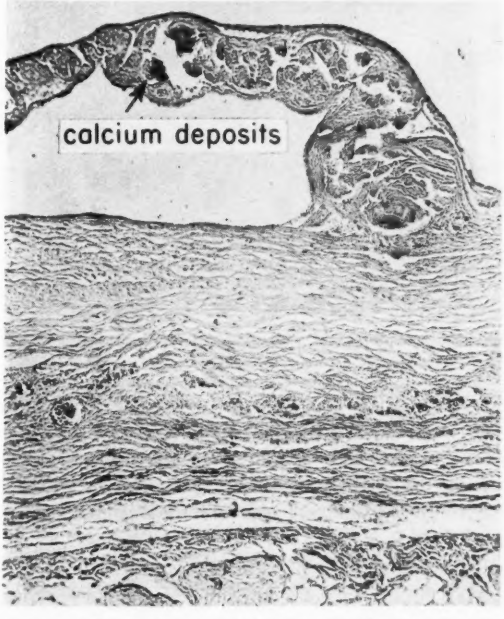

Fig. 7.—Photomicrograph showing organizing granulation tissue containing calcium deposits and the scarred epicardium. The animal died seven weeks after injection of blood lipid fraction into pericardial sac.

Microscopically, the areas of patchy pericardial thickening showed inflammatory reaction and scarring with dense collection of phagocytes filled with blood pigment (see Fig 3).

Animals who had the blood lipid fractions injected all showed more advanced changes. Those changes consisted in pericardial and epicardial thickening, patchy areas of granulation tissue, and adhesions. The changes were more advanced in the animals which were sacrificed at longer intervals (see Fig. 4). No evidence of pericardial effusion or remnants of the injected lipid suspension were found free within the pericardial sac.

Fig. 8.—Photomicrograph demonstrating phagocytized lipid material within the scarred epicardium. This is the same animal as demonstrated in Fig. 7. (Sudan III stain.)

One of the animals died at seven weeks with advanced findings resembling Pick's disease due to constrictive pericarditis. Grossly the animal had generalized edema, ascites, and bilateral pleural effusions. The heart was small, constricted, and surrounded by a densely thickened pericardial and epicardial layer. A small amount of hemorrhagic sterile fluid was present in the pericardial space (see Fig. 5).

Microscopically the presence of adhesive pericarditis with slight inflammatory response was found in some of the less-advanced specimens (Fig. 6). In the animal which died of the constrictive pericarditis, extensive inflamma-

tory response and scarring were present. Considerable amounts of organizing fibrin, some of which contained early calcium deposits, were found (Fig. 7). Fat stains (Sudan III) demonstrated phagocytized lipid material within the extremely scarred epicardium and pericardium (Fig. 8).

The two dogs which received crystalline cholesterol suspension injections into the pericardial sacs, sacrificed at six and ten weeks each, showed essentially the same findings as the majority of the dogs receiving the lipid extract. Well-developed constrictive pericarditis was not produced in those animals.

SUMMARY

A review of the literature has revealed several cases which show the sequence of traumatic hemopericardium followed at varying intervals by signs and symptoms of constrictive pericarditis. The patient reported in this presentation adds additional evidence to this line of thought.

A series of dogs received an intrapericardial injection of autogenous dog's blood and a second series injections of the lipid fraction of pooled dog's blood. Only one animal in the latter series demonstrated well-developed constrictive pericarditis. The remainder of the dogs in the lipid series showed lesser changes. The animals in the blood series showed the least changes. These experimental findings are interpreted as supportive evidence that in some instances constrictive pericarditis may be the end result of intrapericardial hemorrhage. It would also appear that the lipid fraction of blood is probably the significant component in the production of pericardial reaction.

This problem is not considered closed until similar experiments have been carried out using repeated injections of blood and lipid fractions of blood to simulate more long-standing hemopericardium.

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DISCUSSION

DR. C. THOMAS READ, Phoenix, Ariz.—Early in our studies of the enzymes in New York, we were asked to see a patient who was practically moribund with Friedländer's pneumonia on the left side. Apparently an empyema of the pericardium had formed and we were asked to investigate this situation relative to the use of the enzymes. We thought this offered an opportunity to study an unusual situation so a small polyethylene catheter was inserted into the pericardial sac by way of a large needle of about 12 to 13 gauge. When the catheter was in the pericardial sac, the needle was removed. The catheter was then attached by way of another smaller needle (cannulated within the catheter) to a three-way stopcock. The catheter was left in situ for a period of thirty-six hours, and the three-way stopcock was put there in order that, if evidence of a tamponade existed, relief of pressure could be carried out. The original specimen of material aspirated was frankly purulent and thick. Upon about three treatments with the enzyme material, an almost serous fluid was the end result. In this situation, whether it was the treatment of the tamponade, or the purulent pericarditis, we do not know; the patient made a recovery so far as the pericardium was concerned. I offer this method as another way in which hemopericardium might be managed.

DR. MARK M. RAVITCH, Baltimore, Md.—As Dr. Ehrenhaft stated, Dr. Elkin, Dr. Bigger, and others have been interested in pericardial aspiration of acute traumatic tamponade, and Dr. Blalock and I have now a series, with the house staff, of 18 or 19 cases of acute traumatic pericardial tamponade, treated with aspiration. As Dr. Ehrenhaft indicated, the citizens who are the subjects of such injuries have a certain self-interest in remaining unavailable, and we have been able to trace only four of our patients who have been intensively studied by Dr. Robert Mason. None of them had aneurysms, none had constrictive pericarditis, and none had electrocardiographic abnormalities. We have had the opportunity to explore the pericardium in only one patient after what appeared to be a successful aspiration. This was a man who was shot through the heart. His electrocardiogram, taken almost as soon as he arrived at the hospital, was diagnosed as showing a block of the anterior descending coronary artery. He did have pericardial tamponade. All his indices were reversed by the aspiration treatment. He died in cardiac failure within a couple of hours. Autopsy showed the injury to the coronary artery and only two or three cubic centimeters of blood at the bottom of the pericardium.

We have had in Dr. Blalock's series of constrictive pericarditis, one patient who had a very severe crushing injury to the sternum years before, who appeared to have a typical chronic constrictive pericarditis. However, we have a clinical observation which leads me to ask Dr. Ehrenhaft a question about the case which he is reporting. This was a Negro who was stabbed through the left chest, had a typical pericardial tamponade which was dramatically relieved by the aspiration of blood, who was admitted to the hospital and stayed

there for several days, when the tamponade returned slowly. The pericardium was aspirated, re-aspirated, and aspirated again, and it soon became apparent that this was bloody fluid and not blood, that he was not leaking from the heart, and a more careful check showed that he had active apical tuberculosis on the left and, in fact, he turned out to have a tuberculous pericarditis. That man may well go on to develop a chronic constrictive pericarditis. We presume that the wounding instrument either went through the lung or, possibly, through a tuberculous mediastinal lymph node, and it was interesting to me that Dr. Ehrenhaft's patient did have some sort of pulmonary difficulty.

DR. ADRIAN LAMBERT, Jr., New York.—I recently had occasion to operate on a patient with chronic hemopericardium of approximately three years' duration. The cause of this was unknown. He had had for the last year symptoms of cardiac tamponade that were relieved by aspiration, which had become ineffective for the last three weeks, just before our exploration. At the time of operation, in spite of vigorous supportive treatment, he came to the operating table with marked anasarca. On opening the pericardium approximately 800 c.c. of chronic fibrinous bloody sludge was removed with old blood. As to the etiology of the hemopericardium, the cause is still unknown.

It was felt, because of the anasarca, that the patient preoperatively was suffering from constriction of the inferior vena cava as well as the cardiac tamponade, and at operation this was borne out. Over the visceral pericardium there was a plaque that was approximately 4 millimeters in thickness. Removal of this in one area was attempted but the heart muscle was so thin and edematous that the heart itself was perforated. This was controlled by resuturing the plaque, after which, as the patient suffered no untoward effects, the inferior vena cava was freed of its surrounding membrane. Following this the heart went into marked dilatation, in spite of the fact that the plaque was still present over its musculature. Arrest of the heart followed, which was relieved by manual massage so that permanent dilatation did not result. In retrospect, therefore, it was felt that the fact that we had not removed the plaque had actually saved the patient's life. This brings up the point whether, in these cases of constrictive pericarditis associated with tamponade, it might not be better, if there is constriction of the inferior vena cave, to free that first so as to avoid dilatation that cannot be controlled, reserving removal of the visceral plaque for a later date if constriction is not completely relieved.

DR. ALEXANDER ADA, New York.—In March, 1948, I had the opportunity to observe a patient who had a pericardial effusion. In the previous five months he had received three distinct contusions of the anterior chest wall. The notable findings on examination were dyspnea, cyanosis, distention of the neck veins, and an enlarged heart. The venous pressure was 290 mm. of saline. Pericardial tap performed in December, 1947, produced 400 c.c. of blood. The diagnosis of hemopericardium was made and, due to the persistence of the latter and the possibility of a neoplastic process or a vascular lesion, pericardiotomy was advised.

At operation the pericardium was found to be bulging, definitely thickened, and lined throughout by fine vascular granulations which bled easily on contact. Large plaques of fibrin were present in the pericardial sac, and there were adhesions between the visceral and parietal pericardium. I felt that the pathologic process present would eventually lead to a constrictive pericarditis, therefore a resection of the anterior two-thirds of the pericardium was performed. This also facilitated drainage of the pericardium into the mediastinum. The pathologic diagnosis was "chronic fibrous pericarditis with old and recent hemorrhage."

This is the first time, to our knowledge, that pericardiectomy has been performed for this particular lesion. Due to the increasing incidence of trauma to the chest, hemopericardium will occur more frequently and may escape diagnosis. Unquestionably, in a large number of these cases, the blood is absorbed without any apparent residual damage. On the other hand, untreated chronic hemopericardium will eventually lead to constrictive pericarditis.

Dr. Ehrenhaft and Dr. Taber are to be commended for their investigation of this particular problem and for bringing to our attention another etiologic factor in the production of pericardial constriction.

DR. EHRENHAFT (Closing).—We have not had occasion to try clinically or experimentally the treatment with enzymes, but I think it should be tried. If one reviews the literature one finds several cases of traumatic hemopericardium and constrictive pericarditis, and one is impressed that there are sometimes years between the time of injury, if it can be elicited from the history, and the evidence of constrictive pericarditis.

In answer to Dr. Ravitch's discussion, I think that the injury in this patient and the hemopericardium are difinitely related to each other, and not to be bronchopleural-cutaneous fistula following drainage of a lung abscess at the age of 4 years.

I feel as Dr. Ada does that in these patients pericardiectomy should always be done. I did not want to bring up the question of aspiration treatment versus pericardiotomy.

RUPTURE OF THE ESOPHAGUS

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TULSA, OKLA.

SPONTANEOUS rupture of the esophagus was first described in 1724 by Boerhaave.[24] From that time up to December, 1950, there were described in world literature ninety-two cases.[40] Eighteen of these individuals survived.[3, 4, 7, 10, 17, 18, 21, 22, 24, 27, 31, 34, 41] In 1951 there were, to my knowledge, twelve additional cases reported,[8, 14, 25, 37, 40, 41, 44] eight of whom survived. It is the purpose of this paper to report four additional cases and to discuss problems associated with the etiology, diagnosis, and treatment of this condition.

In 1944 Graham[21] described two cases that survived following surgical drainage of the pleural cavity. The first case that survived following thoracotomy and repair was reported in detail by Barrett[3] in 1946. The first clinical diagnosis made before death is credited to Meyer in 1846.[24] Even though this condition has been recognized for over two hundred years, the successful treatment has occurred largely in the past five years.

Relatively little has been written on this subject, and even now many physicians are unaware of its existence. Articles and textbooks reviewing the differential diagnosis of acute surgical emergencies often fail to mention rupture of the esophagus. Rupture of the esophagus probably occurs more often than is suspected. This condition should, therefore, be the subject of continued scrutiny.

CASE REPORTS

CASE 1.—H. W., a 51-year-old white man, was admitted to St. John's Hospital, Tulsa, Okla., at 9:40 P.M. on Nov. 25, 1950. The patient stated that he noted, while eating dinner at about 7:15 P.M., that he had a sensation of something "backing up into his throat." He took several swallows of water, in an attempt to wash the bolus of food down, with no effect. He felt a substernal pain that followed the last swallow of water. This was followed by a severe midepigastric pain which lasted for several minutes and was then partially relieved. In about twenty minutes the pain recurred and was extremely severe. It had persisted from this time until the time of the examination. There was no retching or vomiting.

Past history revealed symptoms of peptic ulcer for which he had been under treatment. He had failed to confine himself to his ulcer regime. He was known to eat poorly, and consumed rather large quantities of alcoholic beverages. Roentgenograms in May of 1950 showed an active peptic ulcer.

Physical examination revealed a well-developed, well-nourished man. He was lying on his right side with his knees drawn up. He was not in shock. He had previously received ¼ grain of morphine sulfate. His blood pressure was 128/78, pulse 112, respirations 28, and temperature 100.2° F.

Examination at this time was essentially negative except for the following findings: there was marked rigidity in the midepigastric region with mild tenderness. There was

Read at the Thirty-second Annual Meeting of the American Association for Thoracic Surgery at Dallas, Texas, May 8-10, 1952.

slight tenderness throughout the remainder of the abdomen. The lungs were negative to auscultation and percussion. There was no subcutaneous or mediastinal emphysema noted. Roentgenographic examination at this time revealed no air beneath the diaphragm and the chest was clear. No mediastinal emphysema was noted. A diagnosis of possible perforated ulcer was made, and a Levine tube was inserted and constant suction applied. Intravenous fluids and penicillin were given.

On November 26, the red blood count was 4.6 million, with 14.3 Gm. of hemoglobin. The white blood count was 22,300 with 94 per cent polymorphonuclear leukocytes. The serum amylase was 87 mg. per cent at 10 A.M. and 122 mg. per cent that evening. Urinalysis was normal.

On November 27, a roentgenogram of the chest revealed a pleural effusion on the right. Aspiration revealed a bloody, turbid fluid. It contained 18,400 red blood cells, 14,300 white blood cells, and was negative for free or combined hydrochloric acid. A diagnosis of rupture of the esophagus was made.

On November 28, a barium swallow was carried out which showed a defect in the esophagus in its lower third. Surrounding this was a mediastinal abscess, with free air in the mediastinum. Subcutaneous emphysema was felt in the left supraclavicular area. Aspirated pleural fluid was positive for hydrochloric acid. The patient's condition remained the same, although he complained of increased substernal pain, and pain over the posterior portion of the right chest.

On November 29, the patient was taken to surgery and a posterolateral thoracotomy incision was made over the ninth rib on the right side. The thoracic cavity was entered, and a good exposure to the lung and esophagus was obtained. The thoracic cavity was partially filled with sanguino-purulent fluid. The fluid was evacuated, the lower and middle lobes of the right lung were decorticated and re-expanded. However, after some difficulty a longitudinal slit, approximately 1½ cm. in length, was found on the anterior surface of the esophagus lying approximately two inches above the diaphragm. This perforation was closed in two layers, using black silk interrupted sutures. The thoracic cavity was thoroughly cleansed, and penicillin and dihydrostreptomycin were instilled into the thoracic cavity. The lung was re-expanded. The incision was closed with interrupted chromic catgut. Two large catheters, one posteriorly and one anteriorly, were left in place to facilitate drainage of the pleural space and mediastinum.

The individual had a somewhat stormy convalescence. The stomach was kept decompressed by means of a Levine tube and the patient was fed parenterally, receiving blood, plasma, protein hydrolysates, and glucose in Hartman's solution.

The total proteins on Dec. 12, 1950, were 5.12 Gm. per cent, with the albumin 2.49 Gm. per cent and globulin 3.23 Gm. per cent. Although subsequently the protein rose, the reversal remained.

Tube feedings were started on the seventh postoperative day, and gradually increased daily. Because of distention and nausea, the Levine tube was left in until the fourteenth postoperative day. Because of loculated effusion and clinical evidence of a localized mediastinitis, the intrapleural catheters were not removed until the fifteenth postoperative day.

He continued to improve, and was given diet by mouth on December 12. The patient was discharged on an ulcer diet on Dec. 24, 1950, which was twenty-five days following the operation. He has remained well up to the present time, and works every day. He is still on a restricted diet because of his ulcer history. He has a normally functioning esophagus, and barium swallow reveals no deformity.

CASE 2.—V. McC., a 48-year-old white man, was admitted to St. John's Hospital, Tulsa, Okla., on March 6, 1950. At about 3 A.M. on March 6, 1950, this patient had a sudden onset of severe epigastric pain preceded by severe vomiting. He gave a previous history of having had digestive disturbances for which he frequently took soda. He had not been eating or drinking heavily before the onset of this episode, and gave no history of having been a heavy consumer of alcoholic beverages. At 6:30 A.M. the patient took a small drink of

water which was followed by a severe pain similar to the previous one. The patient was admitted to the hospital at 9 A.M., at which time his temperature was 100.4° F., pulse 124, and respirations 24.

Physical examination revealed the patient in severe pain. He was warm and moist, and had no symptoms of shock. Respirations were rapid and shallow. There was a tachycardia without thrills, murmurs, or irregularity. The lungs showed a slightly diminished tactile fremitus in both lower lung fields posteriorly, together with tubular breathing. No evidence of free fluid in the chest was found at this time. The abdomen was rigid with generalized tenderness. The peristalsis was diminished.

His blood count upon admission was 5.2 million red cells with 15.6 Gm. of hemoglobin, 17,650 white blood cells with 95 per cent neutrophils. The urine was normal. Roentgenogram upon admission showed no air beneath the diaphragm. Roentgenogram of the chest at this time showed evidence of fluid in the left thoracic cavity.

By 3 P.M. the epigastric pain had progressed into the anterior chest and was causing dyspnea with cyanosis. Temperature had risen to 101.8° F., the pulse was 124, and respirations 44. At 9 P.M. there was evidence of subcutaneous emphysema noted over the supraclavicular areas, face, neck and anterior chest wall.

The patient was given morphine, oxygen, penicillin, intravenous fluids and aureomycin.

On March 8 the patient's condition was still precarious, and consultation was sought. The consultant made a diagnosis of spontaneous rupture of the esophagus. The only treatment advised was a thoracentesis. The patient was taken to surgery, and a catheter was introduced into the thoracic cavity on the left and attached to an underwater drainage bottle. The Levine tube was used to give the patient tube feedings.

On March 9 the pleural fluid was tested for hydrochloric acid and proved negative. Roentgenogram still showed massive effusion in the left chest.

On March 14 the blood count showed 4.85 million red blood cells and 12,900 white blood cells, with 85 per cent polymorphonuclear leukocytes. The blood amylase was normal. The total protein was 5.77, with the albumin being 2.81 and globulin 2.96 Gm. per cent. The chlorides and CO_2 combining power were normal. The left chest showed massive effusion.

On March 18 bismuth introduced by mouth was found by roentgenogram to be in the left thoracic cavity. Left pleural effusion was still present.

On March 22 the patient was discharged with a diagnosis of ruptured esophagus and empyema.

On March 24 thoracotomy was carried out in Dallas, Texas, by Dr. Robert R. Shaw. A perforation of the esophagus was found immediately above the diaphragm. This was repaired, the lung was decorticated, and the empyema cavity drained. Recovery was uneventful, and the patient was discharged in twelve days.

The patient has done well since, and is now completely well.

CASE 3.—S. F., a 59-year-old white man, was admitted to the service of Dr. A. Ray Wiley, Hillcrest Hospital, Tulsa, Okla., on Oct. 12, 1950. Two hours previous to the time this patient entered the emergency room, he was sitting in a cafe, eating. He noticed, shortly after eating, that there was swelling of his eyelids and that his face was puffed up. This phenomenon continued and, after a short while, was associated with a severe cramping abdominal pain. He became progressively more short of breath. At the time he was seen in the emergency room he was in shock. He was complaining of severe cramping abdominal pain and shortness of breath. There had been no vomiting at any time.

His past history revealed he had had some difficulty in eating and swallowing for the past three weeks. There was also a history suggestive of peptic ulcer in the past. He was known to be a chronic alcoholic.

Physical examination revealed a well-developed, well-nourished man in shock and acute pain. He was cyanotic. There was subcutaneous emphysema around the eyes and eyelids, the face, neck, and the upper and anterior portion of the chest wall. There were bubbling chest râles throughout both lung fields; however, breath sounds were heard throughout. The sounds were diminished somewhat on the right side. The respiratory rate

was 40. He had an irregular pulse of 108. The heart showed no thrills and there were no murmurs noted. His blood pressure was 132/90. The abdomen was rigid and tender throughout.

Laboratory data showed a red blood count of 4.2 million, white blood count of 10,200, with 79 per cent polymorphonuclear leukocytes. The urine was not abnormal. Roentgenograms taken of chest and abdomen on this date reveal the presence of subcutaneous emphysema and mediastinal emphysema. There was no evidence of pneumothorax, atelectasis or fluid in the pleural cavity at this time. A diagnosis was made of ruptured viscus, probably esophagus.

The patient was given oxygen, morphine, and antibiotics. A Levine tube was introduced into the stomach and constant suction established. He was given blood and fluid intravenously. Conservative treatment was carried out over the next nine days. The patient received intravenous fluids, blood, stimulants, and intramuscular injections for pain.

On Oct. 14, 1950, fluid was seen by roentgenographic examination in both bases. There was more fluid on the right side and honeycombing of the lung occurred suggesting pulmonary edema, possibly on the basis of cardiac decompensation. Fluid was removed from both right and left thoracic cavities by thoracentesis. Further roentgenographic examinations of Oct. 20, 1950, showed the subcutaneous emphysema gone as was most of the pleural fluid. Some fluid remained in the left base. By barium swallow a diagnosis of hiatus hernia was made. No esophageal perforation was demonstrated.

The white blood count rose to 38,000 with 93 per cent polymorphonuclear leukocytes. The total serum proteins were 5.5 Gm. per cent on October 21, the albumin being 1.65 Gm. per cent and the globulin being 3.85 Gm. per cent.

On Oct. 21, 1950, the aspirated pleural fluid contained hydrochloric acid for the first time. The x-ray revealed an increase in the fluid on the left. A diagnosis was made of a ruptured esophagus or a rupture of a portion of the stomach contained in the hiatus hernia.

On October 22, the patient was taken to surgery and an operation was carried out by Dr. A. Ray Wiley and Dr. R. M. Shepard. Through a left thoracotomy incision, a foul-smelling empyema was entered and drained. The lung was decorticated and a rent in the esophagus was found 1 cm. above the diaphragm. This was closed with interrupted cotton sutures, the lung re-expanded, and the chest closed with an anterior and posterior drain in place.

The patient did satisfactorily after operation. However, one week after the thoracotomy the ruptured esophagus reopened and an esophago-pleural-cutaneous fistula was formed at the posterior drainage site.

The patient was discharged from the hospital on November 31, 1950, with a posterior drainage from the esophageal fistula but otherwise in satisfactory condition. He continued to do well, with his fistula draining very little. Recent follow-up is not available.

CASE 4.—J. H., a 55-year-old man, was admitted to Hillcrest Hospital, Tulsa, Okla., on March 2, 1949. His chief complaint was inability to swallow. He had had this difficulty off and on for the past three months and, for the past eight weeks, had taken nothing but liquids. He had lost about twenty pounds. He had had some "heartburn" and substernal discomfort.

His past history revealed that he has had a history of trouble with swallowing for six years. In June, 1948, a biopsy of the esophagus had revealed the presence of a mild esophagitis.

On physical examination, this patient was a well-developed, poorly-nourished man who gave the appearance of being in constant distress. An examination of the chest revealed it to be clear to auscultation and percussion. The respiratory rate was 16. The heart was regular without thrills or murmurs, not enlarged, and his blood pressure was 110/90. The pulse rate was 68. On examination of the abdomen, the liver was found to be greatly

enlarged, extending four fingerbreadths below the costal margin. It was smooth and not tender. The spleen was not enlarged, and the abdomen showed no evidence of masses, scars, tenderness, or ascites. Thorough examination revealed no other abnormalities.

Barium swallow at this time revealed an irregular obstruction involving the lower third of the esophagus extending to within one inch of the cardia. The esophagus above was slightly dilated. The urine was normal. There were 4.42 million red blood cells and 13 Gm. hemoglobin. White blood count was 6,600 with 63 polymorphonuclear leukocytes. The blood sugar was 92.1 mg. per cent, the prothrombin 91 per cent, the total protein 4.7 Gm. per cent, and the chlorides were 679 mg. per cent. The albumin-globulin ratio was not done.

Because the patient was unable to take sufficient food by mouth and because dilation of the esophagus at this time seemed hazardous, he was advised to have a temporary gastrostomy followed later by esophageal resection or dilatation. This he refused, so on March 3, 1949, the patient was taken to surgery. A No. 8 × 45 esophagoscope was introduced down to a level just below the aortic arch. At this level it was noted that the mucosa of the esophagus was extremely red and edematous and the scope was inserted no further. Nos. 10 and 12 esophageal bougies were successively introduced over a previously swallowed string. These passed under direct vision into the stomach with no difficulty. Further dilatation was not considered wise.

The patient returned to his room in good condition and later had a lunch of clear liquids. For dinner he had cream soup and other liquids. Both meals were taken without pain or difficulty in swallowing. The next morning he had a soft diet for breakfast and another soft diet for lunch. About ten minutes after his lunch, while sitting up in bed, he had a sudden excruciating substernal pain. He did not vomit.

Examination one hour later showed the patient to be writhing in pain and sweating profusely. His color was good, there was substernal and upper abdominal pain with mild abdominal rigidity. There was no subcutaneous emphysema. The pulse was 100, temperature 99.4° F. and respiration 24. The blood pressure was 110/80. Breathing was difficult.

Within an hour roentgenogram of the chest revealed a collapse of the right lung and fluid within the right pleural cavity. There was no evidence of air under the diaphragm or of subcutaneous or mediastinal emphysema. A large rubber catheter was introduced through the chest wall and into the pleural cavity and suction applied. All food by mouth was stopped and a Levine tube put into the stomach through the esophagus and the patient was put on massive doses of antibiotics, oxygen, and enough morphine to relieve the pain. Under this conservative management, he did reasonably well through March 5. However, on March 6, the patient's condition was apparently deteriorating. Roentgenographic examination at this time revealed further fluid in the pleural cavity and the right lung only partly re-expanded. The drainage from the tube within the pleural cavity appeared purulent.

On March 6, 1949, the patient was taken to surgery and a right thoracotomy carried out, at which time a cleansing of the lung and pleural cavity was accomplished and a small rent at the lower end of the esophagus, approximately one and one-half inches above the diaphragm on the posterior wall of the esophagus was found. The esophageal wall at this point was extremely friable. The hole was closed with some difficulty and a flap of pleura brought over the hole as an additional support. The thoracotomy incision was closed leaving two large drains in place, one anteriorly and one posteriorly. It was felt that the esophagus was in such bad condition that the perforation might possibly fail to close and for that reason a small incision was made in the anterior abdominal wall and a Witzel gastrostomy was carried out.

The patient did reasonably well following this procedure. The lung re-expanded and the patient tolerated the gastrostomy well and gained weight. The red blood count remained normal. The white blood count fell and the total protein rose to 5.5 Gm. per cent. However, on the seventh postoperative day there was an increased drainage

through the posterior drainage tube which had been left in place. Roentgenographic examination at that time revealed that there was a posterior pocket leading from the esophagus out through the pleura and the posterior drainage tube.

The patient continued to do well. However, on March 18, the gastrostomy tube was inadvertently removed and it was impossible to reinsert it. Further need for it was apparent so the patient was taken to surgery and the Witzel gastrostomy re-established and the abdomen closed in the usual manner. He continued to do well and gained weight. He was discharged on March 26, 1949, with a gastrostomy tube in place and a small esophago-pleural-cutaneous fistula posteriorly. The patient was then transferred to a veterans hospital, where he continued to do well.

At the present time he still has his esophageal fistula and is not able to carry on his regular vocation. However, he is up and around and in reasonably good health.

COMMENT AND DISCUSSION

The four described cases have the typical history and physical findings associated with a spontaneous rupture of the esophagus. They are not spontaneous, however, because of the fact that the rupture is associated with disease of, or a change in, the esophageal wall. In two instances the disease of the esophagus was symptomatic. In the other two cases, there was history of peptic ulcer which is often associated with esophagitis. In three instances there is definite history of an inadequate diet and alcoholism. In all four cases there was a disturbance of protein metabolism with a low total protein and a reversal of the albumin-globulin ratio. All of the above factors contributed to a weakness of the esophageal wall.

Only one case was associated with vomiting but the other three were preceded by a large meal or an alcoholic bout. These conditions possibly contributed to increased intraluminal pressure in the esophagus. Two factors are responsible for the rupture in all cases: first, increase in intraluminal pressure, second, further weakening of the esophageal wall.

In none of these cases was definitive surgery undertaken at the proper time. The delay in carrying out a thoracotomy and repair undoubtedly contributed to the postoperative complications and prolonged convalescence in these cases. Fortunately they all survived in spite of delayed treatment. In one instance it is quite likely that the patient would have survived under conservative surgical management but would have been left with an empyema and an esophageal fistula. Thoracotomy and repair in this case restored the lung to its normal physiology and made possible repair of the fistula.

These cases bear out the point that if the patient survives for forty-eight hours, one may be more conservative in his methods of treatment and the patient has a reasonable chance of survival. If the patient is seen in the first few hours one cannot be at all certain that he will survive without surgical repair. They also bear out that thoracotomy and closure of the defect will bring about a more nearly complete and more prompt recovery.

A study of these cases correlated with the cases reviewed in the literature leaves no doubt that thoracotomy with repair is, in every case, the most satisfactory method of treatment.

ETIOLOGY

Rupture of the esophagus following instrumentation or as a result of a foreign body is usually diagnosed without delay.[28, 35, 36] The etiology is obvious and the problems are the same as in rupture of the esophagus from a less obvious cause.

Rupture secondary to neoplasm or long-standing disease offers a different problem. The remarks in the paper will be largely confined to "so-called" spontaneous rupture of the esophagus.

"Spontaneous rupture" means rupture of the esophagus that is presumably normal before the perforation occurs and not caused by an external force. It is not associated with disease in or around the esophagus, with a foreign body in the esophagus or with manipulation of the esophagus.

The etiology is undecided and many ideas concerning it have been put forth.[1, 13, 16, 19, 24, 26, 39, 44, 47] McKenzie, working on human cadavers in 1848, noted that it required 5¾ to 11 pounds pressure per square inch to rupture the esophagus of an adult, the average being approximately seven pounds per square inch. Other investigators have similar results.[24] It was also pointed out that the rupture nearly always occurs in the terminal three or four inches of the esophagus which experimentally represents the weakest portion of the esophagus.[24, 29] It is the rapidity of the rise in intraluminal pressure rather than the total degree of pressure that is the most important factor in the cause of perforation.[24]

It is interesting to note that these observers found that the esophagus of a child would resist more pressure than that of an adult. It requires approximately four times as much pressure to rupture the esophagus in a child below twelve years as it does to rupture an adult esophagus.

From an anatomical standpoint, certain other observations by Mosher[30] are significant. These points are: (1) Esophageal muscles at the lower end terminate in a conical fashion, the tapered end being extremely thin, (2) an inherent weakness exists at the site of entrance of the vessels and nerves into the musculature at the lower end of the esophagus, (3) the esophageal muscles at the lower end are relatively weaker than the muscles of the stomach, and (4) segmental defects are found in the circular muscle layer at the lower end of the esophagus in some of the cadavers dissected.

Beattie[6] noted experimentally that electric stimulus of the tuber cinereum in animals caused a hyperperistalsis in the stomach together with hyperemia of its mucosa. This may be significant in accounting for the severe vomiting and occasional rupture of the esophagus that is found in patients with intracranial disease.[13, 23, 40]

Kinsella[24] reviewed six circumstances in which rupture may occur. All of these imply either a change in the esophageal wall or the application of a force. A review of many cases in the literature brings out the facts that not a few of the cases have a history suggestive of peptic ulcer, many are chronic alcoholics, and some are in a poor state of nutrition from various causes. These conditions may imply changes in the esophageal wall. The fact that, with one exception,

the rupture occurred in that part of the esophagus that experimentally or anatomically proved to be the weakest would lead one to believe that force plays an important part. One should not lose sight of the fact that disease is also more common in this lower portion.

Since circumstances imply that both force and previous changes in the wall of the esophagus have a major role in the cause of this condition, as suggested by Samson,[41] the word "spontaneous" is a misnomer. Since the term "rupture" means perforation by force it is ill used with the word "spontaneous."

The term "postemetic" may accurately be used to describe many of these cases. However, three out of our four cases did not vomit, and several cases in the literature failed to vomit. Vomiting only *after* the severe pain following the perforation is reported several times. This suggests that the vomiting may be the result of the rupture in some cases, and not the cause. Vomiting causes rupture of the esophagus by a sudden increase in the intraluminal pressure. It has been suggested that this increase in pressure usually occurs when the stomach is full and therefore the pressure cannot be released into the larger lumen of the stomach.

In the cases reported in this paper it was noticed in each case the total proteins were low and there was a reversal of the albumin-globulin ratio. The significance of this is not known.

It is suggested, in summary, that rupture of the esophagus is caused by a sudden increase in intraluminal pressure. Nearly all of the reported cases show positive or suggestive evidence of pre-existing disease in the esophagus. Such disease may have been asymptomatic before the perforation occurred. Poor nutrition or disturbance in protein metabolism may weaken the esophageal wall.

PATHOLOGY

Rupture of the esophagus is most frequently seen on the posterolateral wall of the left side in the lower eight centimeters of the organ (10 per cent on the right side[24]). The tear is usually vertical and may be from 2 mm. to 8 cm. long. If the tear involves the stomach wall, severe bleeding may occur. Perforation of the middle third of the esophagus has been described only once (by Fitz) in a paper by Priviteri and Gay.[40] Complete disruption of the esophagus was described in the original case by Boerhaave[15] and again by Higginson and Clagett.[22]

In true spontaneous rupture of the esophagus no disease process, either gross or microscopic, is demonstrable at the site of the tear. Changes that are seen are often thought to be the result instead of the cause of the rupture. It seems more often than not that they are the cause of the perforation.

Tears of the esophagus have occurred in patients with poliomyelitis,[24] meningitis,[20] paresis,[19] intracranial hemorrhage,[40] history of weight lifting,[40] roentgen examination of the gastrointestinal tract,[23] defecation,[40] administration of anesthesia,[40] pregnancy,[45] and brain tumor.[13]

HISTORY OF THE DISEASE

This condition is usually seen in men (86 per cent)[15] between the ages of thirty-five and fifty-five years. The youngest reported case was two years,[7, 36]

and the oldest was seventy-five years old.[10, 23] These patients may be well nourished and may have enjoyed relatively good health previously. A majority of the cases, if closely questioned, will reveal suggestive or positive evidence of gastrointestinal upsets and a history suggestive of peptic ulcer. Often these cases are chronic alcoholics and for that reason or some other reason have not eaten a well-balanced diet.

The onset of the disease is marked by a sudden, severe pain. This may be preceded by vomiting, it may be followed by vomiting, or, in some instances, is not associated with vomiting. The pain may be substernal, epigastric, or abdominal and, characteristically, is so severe that large doses of narcotics are required to relieve it.

Within a few minutes to a few hours, the epigastric or abdominal pain will become substernal. It occasionally will radiate around into the back and between the scapulae. Pleural pain may occur on either side. The attack is often preceded by a large meal or by an alcoholic bout. The patient may point out rigidity of the abdomen, particularly the upper abdomen. There is often definitely a discrepancy between the abdominal rigidity and the abdominal pain.

These patients may be in shock, and complain of difficulty in breathing. The degree of cyanosis and dyspnea depends on the severity of the pain and the presence or absence of fluid in the chest, of tension pneumothorax, and of mediastinal and subcutaneous emphysema. The state of shock depends upon the degree of pain, the presence of hypoxia and the amount of blood loss. Extreme thirst is a common symptom.

PHYSICAL EXAMINATION OF THE PATIENT

When the patient is first seen he appears severely ill and is often lying on his side with his knees drawn up. He is dyspneic and may be cyanotic. Shock may be present. The pulse is often not greatly elevated, usually between 90 and 100. The temperature of the first few hours runs between 99 and 100 degrees, the respiratory rate is always rapid, being between 30 and 40, and the blood pressure is usually normal, but may be quite low.

Examination of the skin and subcutaneous tissue often reveals evidence of subcutaneous emphysema. This may be generalized but is often first noted in the left supraclavicular area, the right supraclavicular area or at the suprasternal notch. It is often noted over face and neck and only rarely over the anterior chest wall.

Examination of the chest may be entirely negative. However, if pleural effusion is present, the typical findings of lack of breath sounds and dullness over the area of the effusion can easily be noted. This usually occurs on the left, but may occur on the right side or bilaterally. In 71 cases reviewed by Priviteri and Gay[40] 91 per cent had a hydrothorax or hydropneumothorax, and 66 per cent showed subcutaneous or mediastinal emphysema or both (Table I).

The abdomen always shows rigidity, particularly in the upper abdomen, and the disease is often thought to be in the abdominal cavity. This has led to the

misdiagnosis of a ruptured intra-abdominal viscus with a resulting laparotomy. Peristalsis is always reduced. The examination of the abdomen otherwise is negative.

The remainder of the examination is usually of no particular significance. One may note changes in the reaction of the pupils if the patient has had narcotics for the relief of pain. The reflexes are hyperactive throughout.

LABORATORY EXAMINATION

Examination of the blood will nearly always show an elevation of the red cell count due to dehydration. Occasionally anemia is noted because of hemorrhage secondary to the rupture. Ordinarily such a change in the blood count has not had time to occur even though bleeding may be severe. The white blood count shows a slight relative increase in polymorphonuclear leukocytes with leukocytosis.

A roentgenographic examination of the chest taken in the lateral decubitus and/or upright position will reveal no air under the diaphragm. This is an extremely important finding because no case of rupture of the esophagus has shown air beneath the diaphragm.[40] The chest roentgenogram will often show fluid and free air within the pleural cavity. Subcutaneous emphysema may be a prominent finding in the chest roentgenogram. A fluid level or emphysema within the mediastinum is pathognomonic (Table I).

TABLE I. FINDINGS IN EIGHTY-SEVEN CASES OF RUPTURE OF THE ESOPHAGUS

Hydrothorax	85%
Emphysema	62%
Hydrothorax (Left only)	60%
Hydrothorax (Rt. only)	33%
Hydrothorax (Bilateral)	7%
Air Beneath Diaphragm	0%

DIAGNOSIS

The diagnosis of this condition can often be made with ease from the history and physical examination. A diagnostic triad has been emphasized by Barrett and others.[3, 4, 9, 12, 15] This triad is: (1) Rapid respiration, (2) abdominal rigidity, and (3) subcutaneous emphysema. Kinsella[24] states that the diagnosis can sometimes be made over the telephone.

If the diagnosis is in doubt, other diagnostic proceedings may be carried out. These consist of aspiration of the fluid within the chest cavity. This fluid may be turbid or blood stained. It should be tested for food particles and hydrochloric acid. If either is present, the diagnosis is further substantiated. Often the odor of the fluid is important. A swallow of barium or lipiodol followed by fluoroscopic and roentgenographic examinations will often outline the perforation or show a periesophageal pocket with direct communication into the pleural cavity.

If one is still in doubt, dye can be taken by mouth and recovered in the intrathoracic fluid, thus establishing the presence of a fistula between the esophagus and pleural cavity.

DIFFERENTIAL DIAGNOSIS

Ruptured esophagus is most frequently confused with ruptured peptic ulcer, acute pancreatitis, or coronary thrombosis. In addition to these, this condition may simulate mesentery thrombosis, dissecting aortic aneurysm, pulmonary embolism, spontaneous pneumothorax, rupture of a bronchus, volvulus, intestinal obstruction, strangulated bowel, rupture of a gall bladder, and diaphragmatic hernia associated with rupture of the stomach or bowel. If the patient relates the usual history, exhibits the diagnostic triad mentioned above, has fluid in the chest, and lacks free air under the diaphragm, most of the other confusing conditions can be quickly ruled out. Most diagnostic failures are due to the fact that the examiner is unaware of the symptoms of rupture of the esophagus or simply fails to think of the possibility.

Mesenteric thrombosis, coronary thrombosis, perforated intra-abdominal viscus, intestinal obstruction, strangulated bowel, and volvulus, seldom, if ever, cause fluid in the chest and are never the cause of subcutaneous or mediastinal emphysema, and, therefore, should be easily ruled out if one or both of these conditions are present. Some of these conditions are frequently associated with free air beneath the diaphragm, a finding always absent in esophageal rupture.

Rupture of the gall bladder may cause fluid in the chest and is rarely associated with air beneath the diaphragm; however, it is frequently associated with a previous history of gall bladder disease. There is often an obvious gall stone seen in the roentgenogram and it is never associated with subcutaneous emphysema. Acute pancreatitis can usually be ruled out by determining the level of the blood amylase. Acute pancreatitis never causes mediastinal or subcutaneous emphysema but may cause pleural effusion. It is often associated with severe abdominal pain, rigidity and shock.

Pulmonary infarction or embolus never causes emphysema, but they are often associated with a cough and hemoptysis which are not seen in rupture of the esophagus. Abdominal pain and rigidity are not present. The pain and shock may be severe.

Spontaneous pneumothorax may produce any of these symptoms found in rupture of the esophagus but as a rule does not cause the severe pain or prostration associated with rupture of the esophagus. There is usually a high degree of collapse of the involved lung, and fluid rarely occurs at the onset but makes its appearance in twenty-four to forty-eight hours. Subcutaneous emphysema is rarely seen in this condition.

Rupture of the bronchus may cause severe subcutaneous and mediastinal emphysema with pain. There may be a collapse of the lung with severe dyspnea, shock, and prostration. Fluid formation does not occur as an early finding but may form later.

Neither of the last two conditions mentioned are commonly associated with the symptoms of vomiting, retching, or other gastrointestinal symptoms. They rarely cause epigastric pain and they are never associated with a board-like rigidity of the abdomen.

Rupture of a previously herniated stomach or bowel into the mediastinum with an extension into the pleural cavity may simulate rupture of the esophagus in every respect. Careful fluoroscopic and roentgenographic examinations, during which the patient swallows some barium or lipiodol, will often demonstrate the herniated stomach and suggest the diagnosis. Since the treatment of this condition is the same as the treatment for ruptured esophagus, the differentiation of these two conditions is only of didactic importance. In either case, one is forced to do an immediate operation with closure of the rupture.

PROGNOSIS

The prognosis of rupture of the esophagus is always extremely grave. In a review of fifty-three cases by Kinsella,[24] thirteen died in less than twelve hours, twenty-four in less than twenty-four hours, eight in less than forty-eight hours, and only eight survived over forty-eight hours. Early deaths are due to shock, tension pneumothorax or, possibly, hemorrhage. Later deaths are due to pleural or mediastinal infection. In 1946, Eliason and Welty[15] reported a mortality of 100 per cent in these cases with the exception of the two cases reported by Graham.[21] Thirty of the 108 cases considered in this report recovered. All recoveries followed surgery.

While the prognosis may be influenced by the size and position of the perforation, death is likely to occur unless the diagnosis is made and adequate treatment is carried out at the earliest possible time.

In these days of plentiful antibioties, of the judicious use of blood and fluids, and of prompt surgical intervention, the patient can be offered a far better prognosis.

TREATMENT

Treatment of rupture of the esophagus may be divided into conservative management[12, 16, 37, 45] and radical management,[3, 4, 10, 15, 24, 27, 41] or better, by surgical drainage as compared to thoracotomy and repair. Samson,[41] in his recent article, compares fifteen cases treated by the two methods. Of the fifteen cases treated by thoracotomy, ten survived with lesser morbidity. Only eight of the fifteen treated by drainage survived and these with a higher morbidity. The latter group had more postoperative complications and much longer hospital stay. Of the twelve cases reported in 1951, nine underwent thoracotomy and eight survived. Three who were not operated upon, died. The four cases reported in this paper all underwent thoracotomy and survived.

This condition is one of the definite surgical emergencies. If the diagnosis is not obvious, steps should be taken to establish it immediately. Only those procedures that are absolutely imperative to make a diagnosis should be done. The patient should be operated upon as soon as the diagnosis is established. A thoracotomy and repair of the rupture should be carried out. Nothing is to be gained by procrastination.

The presence of shock should not delay surgery. The shock is treated and the thoracotomy undertaken. With proper anesthesia and controlled

respiration the chest is opened. The pleural cavity should be aspirated and the lung re-expanded. The rent in the esophagus is to be found and closed with two layers of nonabsorbable suture. A feeding tube should be passed down the esophagus beyond the perforation and into the stomach. This may also be used for decompression. The chest should then be closed leaving in drainage tubes at appropriate places to insure complete expansion of the lung, adequate drainage of the pleural space, and direct drainage from the site of repair in case of a breakdown.

The shock in these cases is due to pain, hypoxia, and blood loss. The hypoxia is due to tension pneumothorax, pleural fluid, and poor respiration as a result of pain. Under adequate anesthesia, the patient receives high oxygen intake; with the pain stimulus gone, respiration improves. As the chest is entered, the tension pneumothorax is relieved, the pleural fluid is removed, and the lung is expanded. Before and during surgery, the blood loss is replaced. As the causes of shock are relieved, the patient improves and is seen to tolerate the procedure well.

Postoperative complications are empyema, mediastinitis, and breakdown of the repair. The mediastinum is left open with opportunity for adequate drainage into the pleural cavity and, thus, to the outside. Thorough cleansing of the area around the perforation and of the pleural cavity and use of antibiotics in the pleural cavity as well as systemically are imperative. Prompt and complete expansion of the lung is important in preventing empyema. The repair may break down from the sixth to the tenth postoperative day. If this occurs, drainage of the open perforation is necessary. The fistula thus formed will often close in several weeks.

Following surgery, the esophagus is kept at rest for a week or more and the patient is fed through a Levine tube or parenterally. Gastrostomy is seldom indicated. Because of changes in the tissues at the site of perforation, healing is often retarded and thus requires a longer period before feeding by mouth is safe.

If other complications make thoracotomy intolerable for the patient and a more conservative method of management indicated, it may be undertaken. Shock should be combated with blood and fluids. Drainage should be established to relieve tension pneumothorax and to withdraw pleural fluid. Negative pressure should be maintained to assure complete and rapid expansion of the lung. Narcotics, sedatives, and intercostal block are used for relief of pain. Antibiotics are used in high dosage. A Levine tube or gastrostomy may be employed for feeding and decompression purposes. The esophagus is put at complete rest. If mediastinal emphysema is causing respiratory distress, this can be relieved by making an incision under local anesthesia just above the suprasternal notch through the anterior fascia and muscles of the neck. Through this incision a catheter can be introduced into the mediastinum for decompression.[11]

Should the patient survive for forty-eight hours or more without surgery, more conservative methods of treatment may be satisfactory. In any event,

more conservative methods are often associated with residual fistulae and empyema. These require thoracotomy and correction later.

SUMMARY

1. The etiology, pathology, symptomatology, diagnosis, and treatment of rupture of the esophagus are discussed.

2. It is suggested that the term "spontaneous" is a misnomer in most cases.

3. The findings are typical in most cases and the diagnosis not too difficult. A diagnostic triad is emphasized.

4. Most diagnostic failures are due to lack of knowledge or failure to think of the possibility of rupture of the esophagus.

5. It is felt that the treatment of choice is immediate thoracotomy with closure of the perforation and re-establishment of the normal anatomy and physiology.

6. With early diagnosis and treatment the prognosis is good.

7. Four cases are reported. All were treated successfully.

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DISCUSSION

DR. OSLER ABBOTT, Atlanta, Ga.—I certainly feel that Dr. Anderson is to be congratulated. I also feel very strongly that we owe a tremendous debt of gratitude to our secretary for organizing our thinking in regard to this disease. I hesitate to rise, but I feel in some ways it is my duty when I can add to the series 31 patients with spontaneous rupture of the esophagus. I would like to show slides that exemplify some of the lessons we have learned in this regard.

(Slide.) I think it is important to stress what appears to be practical classification of patients, and there are some things in the symptomatology that are important. These patients are not all in the lower income brackets. The ones in the upper income brackets are oftentimes ulcer patients and have a restricted diet. We had the opportunity, I should say not too much desired, to take care of the brother-in-law of a famous vascular surgeon, and cure him of this disease. The first thing I would like to emphasize with regard to the symptomatology, is that you must listen to the patient, because in going over the history of patients who died or had delayed treatment, they so often give the bizarre history that something ruptured and moved into the chest, or something ruptured in the chest and moved. This is a very important differential diagnostic symptom.

(Slide.) This is from the paper by Drs. Fincher and Swanson on the neurogenic causes of this disease, which appeared in the Annals of Surgery. Of course when you study anything neurosurgical, you look back in the textbooks, and usually find that Dr. Cushing described it in detail thirty years ago. The important thing is that these patients, after mid- or posterior fossa surgery, and possibly a majority of patients who die following neurosurgery, may have this as a complication.

The management of such patients I think requires three things. First, consciousness of the disease; second, any patient following a neurosurgical operation, who has blood in the initial vomitus postsurgery, has this disease; and next, the patient must have ventricular drainage to control the pressure on the tuber cinereum area; and, finally, if they are operated upon transpleurally, there is diffuse disease of the esophagus, and Dr. Torek's T-tube in the esophagus is the answer to this type of patient. I think we should compliment him on that.

(Slide.) This is a typical example of rupture in a neurogenic case and one of the factors of course is weakness of the lower esophageal musculature and the attachment at the diaphragm and periesophageal fibrosis. I think that is important in the mechanism.

(Slide.) One of the things I would like to add to conservative management. In patients who are seen more than 15 hours after onset of the disease, it is valuable to put in multiple thoracotomy tubes and irrigate with saline until the pH of the pleural fluid is within normal limits. This will relieve the secondary shock if the mediastinal pleura is not under tension.

DR. WILLIAM W. HEROY, Huntington, N. Y.—I feel that Dr. Anderson has given us a very clear picture of this interesting problem. I wonder whether these ruptures are really spontaneous, or, for the most part, are the result of underlying disease. It is a bit unclear in my mind why we do not have, in the cases reported, some underlying ulcers. Many of the patients we see with this condition will give histories of chronic pain under the sternum. I would like to show two cases to exemplify this point.

(Slide.) The first case was a 33-year-old chronic alcoholic hotel maid, who was in the habit of drinking large quantities of beer. For lunch she claimed to have had several beers, and returned to work where she developed severe substernal pain. In order to relieve this pain she took a dose of soda bicarbonate and added a little vinegar to make it more potent. Following this dose she was seized with overwhelming pain in the substernal area and was rushed to another hospital, where she was kept for a couple of hours until she vomited about 200 c.c. of blood, and was transferred to us. When she arrived she showed the classic picture of just what she had, in its most severe form with shock and subcutaneous emphysema.

(Slide.) Because of her very poor condition at the time we finally got her, it was elected to wait, and she was given supportive care and very heavy antibacterial therapy. She then went into a toxic psychosis and operative procedure was further delayed until she developed evidence of empyema in the left chest which was explored and drained one week after admission. She did fairly well until a week later, when she developed a cutaneous fistula, and the feedings given by Levine tube dumped out. A gastrostomy was done to control this, but the gastrostomy feedings came out through the fistula. Over a period of the next two weeks the fistula gradually closed, and she made an uneventful recovery. After that, and a year later she had a perfectly normal child. At the time of the gastrostomy the liver biopsy showed fatty disease of the liver.

(Slide.) This simply shows the fistulous tract running out to the chest wall.

(Slide.) This shows the final film.

(Slide.) The second case is a 68-year-old man who, while watching television one night, was seized with severe epigastric pain. There was a history of two weeks of substernal pain, and it was thought that he had a perforated ulcer. He refused hospitalization at first, but finally came in and was explored. The entire abdomen was negative. The esophageal hiatus

was explored with the finger, but the peritoneum was not opened. If you do not open the peritoneal surface and have a collection in that area, it may be missed as it was in this case.

(Slide.) This last slide shows the collection, which was actually well localized between the diaphragm and the pleura, and I think gives the whole picture away. This is emphysema before it has gotten into the mediastinum, before it has entered the pleural space. I would go along with Dr. Anderson 100 per cent that one should look for esophageal perforation and operate early and repair the defect.

I would like to ask him if he does not feel that a great many esophageal perforations have pre-existing and unrecognized underlying ulcers.

DR. RICHARD H. OVERHOLT, Brookline, Mass.—I think we will all agree that it is important to carry out a direct surgical attack on the situation pointed out by Dr. Anderson and do it as early as possible if surgery is required. However, sometimes the surgeon has to make the best terms he can with a difficult situation and cannot control the timing of treatment. I would like to report a rather unusual case in which the etiology was related to acute alcoholism. There was a long interval between esophageal rupture and mediastinal drainage. During this interval, the same liquid that precipitated the rupture was the only nourishment taken and probably favorably influenced the outcome. This patient was on a hunting trip and, because there were no deer the first day, he began drinking. Late in the evening there was some scuffling and wrestling and finally he ended up at the bottom of a pile of hunters. Soon his friends noted marked swelling of his neck and face. Swallowing was painful. On the following day, while the rest of the men went out hunting, he stayed in bed, sipping Scotch whisky. He was there eight days and on the return trip, the patient was so critically ill that his friends took him to a hospital where he remained for four days.

(Slide.) This roentgenogram shows a large air collection and fluid levels on both sides. There was diffuse density in both lung fields, indicating bronchopneumonia.

(Slide.) A barium swallow was given which revealed an esophageal communication with both pleural cavities and a massive bilateral emphysema. Closed drainage was provided after bilateral rib resection and aspiration of purulent material and food contents. Due to the marked inflammatory reaction everywhere, no attempt was made to repair the esophageal defect. There was a rent about 7 centimeters in length. The patient carried and was fed through a Levine tube for 67 days.

(Slide.) There is satisfactory re-expansion of the lung and there has been a check on esophageal function five years later. There is no stricture of any kind. This illustrates that you must not give up on some of these very serious cases, and we have to make the best terms we can with them, regardless of the time factor.

DR. JAMES M. MASON, III, Birmingham.—I have been much impressed with the progress that has been made in the care of perforations of the esophagus since it has been demonstrated that they can be successfully treated by primary one-stage operation.

Sweet has demonstrated that excellent results have followed one-stage closure of esophageal diverticula, and his work has no doubt influenced the one-stage primary closure of esophageal perforations. Many of us have had excellent results with primary closure, whereas late attempts at closure have been disappointing.

DR. HERBERT WILLY MEYER, New York.—I think it is most timely to have heard the excellent paper by Drs. Anderson and Curtis. I would like to report two cases. They are not my own cases as they date back a great many years. In 1940 I had the occasion to look up the literature on perforations of the gastrointestinal tract. In 1724 Boorhaave reported a unique case in which the rent in the esophagus was transverse. The majority of spontaneous perforations of the esophagus are linear. It is important, however, that we keep in mind that spontaneous perforations may also be transverse in direction. This emphasizes Dr. Anderson's advice that early operation is certainly important and indicated.

It is of historic interest also to quote a case by MacKenzie published in his book *Manual of Diseases of the Nose and Throat* (London, 1884). "The patient, Baron de Wassenaer, was 50 years of age and, with the exception that he had a sense of fullness after moderate meals, was in perfect health. To relieve this disagreeable feeling he was in the habit of taking a copious draught of an infusion of 'blessed thistle' and ipecacuanha. One day, about 1:30 in the evening, when he had taken no supper but had had rather a hearty dinner, he was bothered by a peculiar sensation in his stomach, and to relieve this he swallowed three tumblersful of his usual infusion. But to no avail. He then tried to excite vomiting by tickling the fauces. In retching he suddenly felt a violent pain. He diagnosed his own case by saying that there was 'the bursting of something near the pit of the stomach.' He became prostrate and died in 18 hours. At necropsy it was seen that without any previously existing signs of disease the esophagus had been completely rent across in a transverse direction."

There is no question that immediate surgery is indicated in practically every case of suspected or proved spontaneous perforation of the esophagus.

DR. OWEN H. WANGENSTEEN, Minneapolis, Minn.—I rise to a point of definition. The word "spontaneous" still hovers over our concept of this disease. However, I think the evidence is good now that we should capitulate to the title "acid-peptic perforation" of the esophagus. Whereas there are occasional conditions such as Dr. Heroy enumerated, and there are hydrostatic phenomena involved, I submit that *they are quite secondary.* The cecum and the stomach are the two large viscera with large diameters. The stress or tension on any surfaces to which intraluminal pressure is applied is the product of the pressure times the diameter times pi (T [tension] = Pr [pressure] × D × *pi*).

Whereas the fundic end of the stomach or the cecum can be ruptured at pressures of 80 mm. of Hg, it takes more than an atmosphere of pressure to rupture the esophagus (approximately 800 mm. Hg).

If one ligates the pylorus in the dog, maintaining fluid and electrolyte balance parenterally, within four days, perforation of the esophagus was observed in 4 of 8 dogs subjected to this experiment; esophagitis was observed in all the eight dogs; the stomach, as you observed from the slides, was quite normal in all.

Moreover, when acid-peptic juice collected from an isolated dog's pouch was dripped into the esophagus at a maintained ultraluminal pressure of 20 cm. of fluid, a severe esophagitis with perforation always followed. In fact, the cat's esophagus can be perforated within 20 minutes by dripping acid-peptic juice into it under these conditions. (Ferguson and associates, Surgery **28:** 1022, 1950.)

Furthermore, the esophagus also is sensitive to the other digestive enzymes of the upper alimentary tract; even the reflux of bile and pancreatic juice into the esophagus will cause erosion of the esophagus, even after total gastrectomy. In the dog, anemia is observed following this occurrence from the erosive esophagitis. (Cross and associates, Proc. Soc. Exper. Biol. & Med. **77:** 862, 1951.)

Finally, I want to show one of Dr. Harvey Cushing's pictures illustrating an erosive action of the digestive juices upon the esophagus. It is to be remembered that Cushing emphasized the relationship of the interbrain to peptic ulcer in the Balfour Lecture; in fact, that was the title of the lecture (Surg., Gynec. & Obst. **55:** 1, 1932).

I submit: it is the reflux of acid-peptic juice into the esophagus which was the likely cause of the perforations observed by Dr. Cushing.

I think it is time that we delete the word "spontaneous" and call this disease by its rightful name—acid-peptic perforation of the esophagus.

DR. DAVID H. WATERMAN, Knoxville, Tenn.—I rise merely to report six cases of perforation that we have treated. In two of these the diagnosis was confirmed by aspiration of beer from the chest. Insofar as we know, television was not etiological in any of our cases.

I certainly subscribe to the use of immediate exploration. I might say that at the time our cases occurred, however, we were a little more timid about opening the thorax than we are today. In all except the first patient, who died promptly after admission with bilateral pneumothorax and a typical picture of shock, the patients were treated by closed thoracotomy, massive antibiotic therapy, and by later gastrostomy. All five recovered.

DR. J. D. FRYFOGLE, Detroit.—I wish to report a case of unusual spontaneous etiology, and this case was definitely not an alcoholic. I was called to see a newborn baby, a female infant of normal pregnancy and normal delivery, who breathed and cried spontaneously at birth. However, in a very few minutes she became quite dyspneic and cyanotic and efforts at tracheal aspiration and aspiration of the hypopharynx were not successful in relieving the condition. Physical and roentgenologic examination confirmed the diagnosis of tension pneumothorax, which was relieved by needle aspiration. The baby was placed in oxygen and in several hours the crisis again arose. This time more definitive measures were carried out, and a 17-gauge needle, fashioned after the manner of the "S" needle, was placed into the chest under water-seal suction. This seemed to control the respiratory difficulty. The baby was given her first feeding, of plain water, about 12 hours later and another supreme crisis arose, with everything getting black and no breath at all.

I was available at the time, and with a large syringe I aspirated the tube already in the chest and withdrew mucus. I had the horrible thought that I was merely deflating the stomach that was in the right chest. I was proved wrong on both diagnoses, however. We gave the baby a swallow of lipiodol, which transversed a normal length of the normal lumen of the esophagus right down to the diaphragm and then deviated markedly to the right and up into the right chest, so we proceeded with thoracotomy and, opening the baby's chest, we found a total mucoid empyema which occurred at about 12 hours, and a rupture at the base of the esophagus, perforating through the right pleura. I worked through the little hole, to find that there was a web directly across the base of the esophagus which did not even permit air to enter the stomach. Had I been more astute I probably would have recognized that there were no air bubbles in the stomach on the first film. The rent in the esophagus was enlarged, the small web cut out, a tube passed through the nose into the stomach, the perforation was closed, the lung decorticated and the patient did very well.

DR. GABRIEL P. SELEY, New York.—I would like to report an experience with conservative management of a case of ruptured esophagus. This patient was a 64-year-old obese housewife, who presented herself to a gastroenterologist for vague lower abdominal pain. As part of the work-up he attempted to pass an Ewald stomach tube. As he attempted this the patient violently resisted and retched. However, he persisted in his efforts and shortly afterward the patient complained of pain in the lower back. This pain was very severe and of a burning nature. Within the next few hours she experienced increasing pain, especially on swallowing, even swallowing her own saliva. Within six hours she was febrile and the following day was hospitalized and treated by oral sulfonamides and fluids by mouth. The temperature gradually rose until it reached 104° F. and her general condition was serious.

I first saw her on the fifth day. At that time she was quite ill, and the roentgenogram showed a diffuse mediastinal and subcutaneous emphysema and bilateral pleural effusion. Because five days had elapsed we elected to treat this patient conservatively. A bilateral pleural tap was done; clear fluid was obtained from the right side, and cloudy fluid from the left. Penicillin solution was instilled. Smears of the fluid from the left side showed many types of bacteria. There were no bacteria in the right pleural cavity. Penicillin, streptomycin and aureomycin were given parenterally and nothing was allowed by mouth. She was fed intravenously. She had a perfectly uneventful recovery and at the end of one month a roentgenogram with dye contrast medium showed a perfectly normal esophagus.

I merely mention this case because it illustrates a different approach to the treatment of this disease.

DR. ANDERSON (Closing).—I certainly want to thank all the discussors.

With regard to the question about ulcer; in the cases considered in this paper it was difficult, because of the inadequate information concerning the cases, to really know about ulceration. I can say that a few cases had proved ulcers of the gastrointestinal tract, that is, peptic ulcers. In only one case was I able to find mentioned an esophageal ulcer that had perforated. Suggestive evidence of peptic ulcer is common in these cases.

I think it is interesting to hear about the baby with perforation. This perforation was associated with a definite congenital abnormality. Perforations of the esophagus in children are rare for two obvious reasons: (1) they do not have peptic esophagitis, have not had time to develop that; and (2) it takes four times as much pressure to rupture the esophagus of a child under 12 years of age as it does the esophagus of an adult, which may be a factor to substantiate its rare occurrence in children.

So far as treatment of late complications is concerned, I believe there is a time when conservative management is sometimes the management of choice, if the individual is seen several days after the onset and appears to be holding his own. In the case Dr. Overholt mentioned, it appears to me that the man probably could not be killed by anything, after all that. I do not mean that as a reflection on Dr. Overholt's treatment. Nevertheless, I think in some cases one must treat them in a more conservative manner. This phase of treatment will be discussed further in the published manuscript.

THE EFFECTS OF ATELECTASIS ON PULMONARY BLOOD FLOW IN THE DOG

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IT HAS been known for some time that atelectasis of one lung results in diminished blood flow to that lung. In dogs anesthetized with barbital Moore[1] introduced two cannulae into the trachea and left main-stem bronchus by means of a left thoracotomy. After closure of the chest and removal of air from the pleural space, one of the tubes was obstructed while the dogs spontaneously breathed oxygen through the other lumen. Fifteen to seventy-five minutes later, the ratios of flow through the two lungs were computed from mixed venous and arterial blood, assuming full saturation of blood draining the normal lung. Flow through the atelectatic lung amounted to 0 to 42 per cent of total flow. Similar data were obtained by Andrus.[2] The present paper is concerned with a reinvestigation of this problem, studying changes in flow as a function of duration of atelectasis under both acute and chronic conditions. In addition, changes in pulmonary vascular resistance resulting from acute atelectasis were investigated.

METHODS

1. *Acute Experiments.*—A left thoracotomy was done under Nembutal or chloralose-morphine anesthesia on dogs after an intratracheal cannula had been tied in place. Artificial respiration was given by means of a Starling pump. A large tie was placed around the left main-stem bronchus. The pericardium was opened to expose the pulmonary artery. The posterior inferior mediastinal pleura was also incised to expose the right inferior pulmonary vein. The systemic arterial pressure was constantly recorded with a mercury manometer. During a control period of ten to twenty minutes of bilateral oxygen breathing, the oxygen consumption was determined by the conventional spirometric technique. Immediately thereafter, pulmonary artery pressure was recorded by means of a Sanborn capacitance manometer attached to a needle in the pulmonary artery; pulmonary arterial and systemic arterial blood samples were drawn for analysis of oxygen content. The left main bronchus was then occluded by tying the ligature. With the nitrogen washed out by previous oxygen breathing, the lung shrank visibly and was completely atelectatic in three to five minutes. At periods varying from ten minutes to two and one-half hours, determinations of the oxygen consumption and of the pulmonary artery pres-

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This study was supported by a grant from the United States Public Health Service.

Read at the Thirty-second Annual Meeting of The American Association for Thoracic Surgery at Dallas, Texas, May 8-10, 1952.

sure and oxygen content of pulmonary arterial and femoral arterial blood were repeated. In addition, the oxygen content of blood from the right inferior pulmonary vein was measured. It was assumed that this was representative of all of the blood draining the right lung. Oxygen analyses were performed on the Van Slyke-Neil manometric apparatus—duplicate determinations checked within 0.2 volume per cent.[3]

From these data cardiac output and blood flow and vascular resistance of each lung during the period of atelectasis were calculated. The computation is illustrated in Fig. 1, in which the pulmonary circulation is diagrammatically represented. The total flow was determined by application of the Fick principle (first and last equations, Fig. 1). It was assumed that

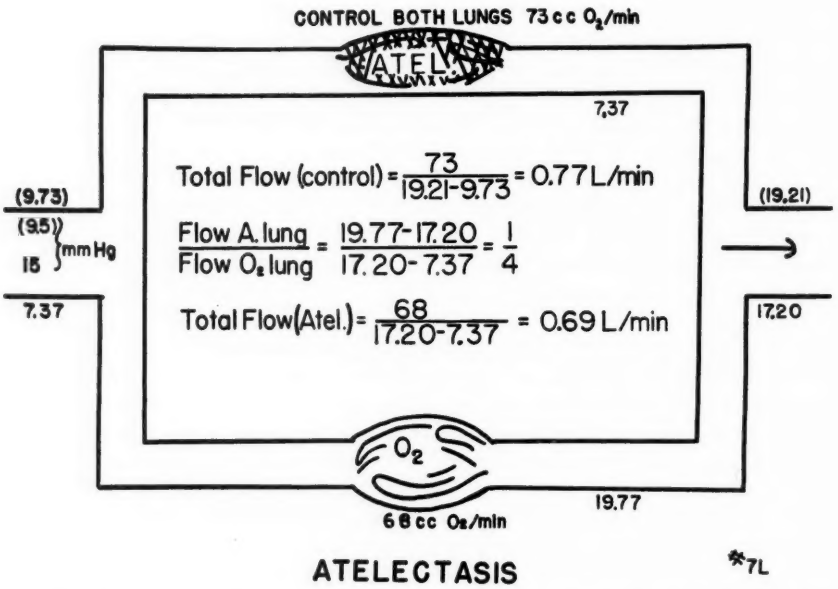

Fig. 1.—Diagram of pulmonary circulation, showing pulmonary artery and its two branches, lungs, two representative pulmonary veins, and a systemic artery. Figures between parentheses were obtained during bilateral oxygen breathing, those without parentheses during atelectasis. The unspecified figures refer to oxygen content (volumes per cent). For calculations, see text.

mixed venous blood passed unchanged through the atelectatic lung. In the nine studies in which pulmonary venous blood from the atelectatic lung was collected as well, this assumption was confirmed. The ratio of flows through the lungs during atelectasis can be calculated from the oxygen content of mixed venous blood, pulmonary venous blood from the oxygen breathing lung, and mixed arterial blood (second equation, Fig. 1). The pulmonary vascular resistance of each lung expressed in arbitrary units was derived by dividing mean pulmonary arterial pressure in millimeters of mercury by the value for flow

TABLE I. ACUTE ATELECTASIS

DOG NO. SIDE	TIME (MIN.)	OXYGEN CONTENT—VOL. PER CENT			OXYGEN CAPACITY (VOL. PER CENT)	SYSTEMIC ARTERIAL O_2 SAT. (PER CENT)	OXYGEN CONSUMP. (C.C./MIN.)	FLOW EXPER. LUNG (PER CENT TOTAL)	CARDIAC OUTPUT (L./MIN.)	PULMONARY ARTERY PRESSURE (MM. HG)		
		SYSTEMIC ARTERIAL	PULMONARY ARTERIAL	RIGHT PULMONARY VEIN						S	D	M
6	C*	14.84	9.33		13.63	>100	79.5		1.44	20	9.2	13
left	40	14.14	9.02		14.88	93.3	74.8	34	1.46	30	13	18
7	C	19.21	9.73		18.41	>100	73		.77	14	8	9
left	50	17.20	7.37	19.77	19.44	87.8	68	20	.69	20	10	15
8	C	16.61	9.92		15.88	>100	117		1.75	23	11	17
left	45	16.00	9.02	16.69	16.58	95.0	67	8	.96	24.1	11	17
	re-expanded	17.28	9.10		15.97	100	103		1.26	23	10	15
9	C	23.34	15.68		21.80	>100	83		1.08	29	10	17
left	65	22.03	16.16	23.15	22.80	95.4	76	20	1.56	26.2	11	17
	re-expanded	22.78	16.64		22.50	>100	70		1.04	22	11	15
10	C	20.36	13.94		18.65	>100	148		2.3	29	10	17
left	10	20.52	13.16	20.29	18.85	>100	140	0	1.9	32	13	20
	60	20.41	13.46	22.41	20.35	99.0	179	22	2.6	34	14	22
12	C						72			32	14	20
left	30	16.89	10.73	19.58	17.90	93.1	90	31	1.46	41	21	26
	120	17.14	10.47	19.8	18.58	91.6	45.6	29	.80	30	13	25
13	C	20.24	16.11		18.30	>100	73.5		1.78	27	13	19
left	45	19.29	14.79	19.52	19.75	96.6	59	5	1.31	32	13	22
14	C	19.32	15.27		17.30	>100	114		2.86	22	12	15
left	40	18.35	15.95	19.18	18.10	>100	129	26	5.3	25	10	14
	50†	18.01	13.28	19.45	18.60	95.6	123	23	2.6	24	12	20
15	C	17.81	13.08		16.80	>100				23	10	15
left	43‡	20.61	12.36	21.71	20.10	>100		12		36	22	29
16	C	18.44	12.36		17.95	>100				19	8	13
left	32	18.56	14.30	22.69	20.60	89.0		49		25	12	15
	45‡	22.56	14.96	22.30	21.50	>100		0		24	12	18
18 left	50	17.73	14.98	19.19	17.80	90.2	109	28	4.3	35	11	21

*Control determination.
†Lung re-expanded between two determinations.
‡Nitrogen breathing before atelectasis.

TABLE II. CHRONIC ATELECTASIS

DOG NO. SIDE	TIME POST-OPERATIVE (DAYS)	OXYGEN CONTENT (VOL. PER CENT)		OXYGEN CAPACITY (VOL. PER CENT)	SYSTEMIC ARTERIAL O_2 SAT. (PER CENT)	FLOW EXPER. LUNG (PER CENT TOTAL)
		SYSTEMIC ARTERIAL	MIXED VENOUS			
85A	C*	12.52	9.12	13.16	93.0	
left	2	11.55	9.09	13.57	85.0	35
	18	7.84	4.81	10.06	77.0	33
6	C	12.30	7.95	13.65	89.0	
left	2	11.77	7.09	14.24	82.0	19
85	C	17.66	13.83	17.97	97.1	
left	3	13.15	6.42	13.78	93.4	8
16	C	13.70	10.00	14.14	95.6	
left	3	16.07	8.81	17.11	92.9	8
	10	15.06	8.50	16.48	90.4	12
	13	10.16	4.87	12.75	81.0	23†
	32	13.54	6.25	14.09	94.9	2‡
	198	12.65	8.84	14.56	89.4	16
C124	C	11.26	6.53	11.97	92.7	
left	2	9.18	4.53	11.40	79.4	26
147	C	17.66	12.32	18.17	96.0	
left	3	13.88	8.43	18.26	75.2	41
	10	12.75	8.01	14.77	85.2	29
	132	15.37	11.70	17.33	87.8	25
	165	12.06	7.11	13.90	86.6	20
12	C	13.76	9.13	16.68	91.1	
left	2	11.09	5.70	13.05	84.2	19
10	C	15.11	11.72	15.69	96.2	
left	1	13.61	7.84	15.03	89.8	12
	5	9.92	5.12	11.31	86.4	17
	8	9.80	3.80	10.58	97.8	0
90	C	11.43	9.08	11.85	96.0	
right	3	12.97	7.09	15.75	81.7	26
76	C	14.51	10.55	15.03	95.3	
right	3	10.03	5.91	12.52	83.8	24
	6	13.23	8.21	14.34	91.2	20
	14	14.26	8.22	15.74	89.7	17
13	C	16.79	11.59	17.40	96.0	
right	5	11.30	6.44	13.92	81.0	32
	12	9.99	7.21	12.01	82.0	39
	33	16.61	11.11	19.91	82.8	38
	41	15.75	8.90	19.46	80.3	32
	51	14.37	8.10	18.36	77.6	35
	55	13.86	9.93	15.36	89.5	22
5	C	13.62	8.18	14.37	93.0	
right	2	11.87	7.30	14.36	82.0	27
	7	11.47	8.99	13.75	82.5	38
15	C	12.12	9.38	12.52	95.4	
right	2	13.29	7.20	14.18	92.5	7
	8	12.90	7.42	13.06	98.0	0

*Control.
†Dog pregnant.
‡Partial pneumothorax on normal side.

through each lung in liters per minute. This assumes that left auricular pressure remains constant and that the pressure drop across the lung is proportional to blood flow.

2. *Chronic Experiments.*—Under Nembutal anesthesia, control right heart and femoral arterial blood samples were drawn for determination of oxygen content and saturation. A right or left thoracotomy was then performed and the main-stem bronchus transected and sutured. At periods varying from two days to six months the blood sampling was repeated. It was assumed that the

TABLE III. CHANGES IN PULMONARY RESISTANCE DURING ATELECTASIS

EXPERIMENTAL NO.	RESISTANCE IN ARBITRARY UNITS*		FACTOR OF INCREASE IN RESISTANCE		
	CONTROL (O_2) LUNG	ATELECTATIC LUNG	CONTROL (O_2) LUNG	ATELECTATIC LUNG	MINUTES
6L	16	20			Control
	20	40	1.25	2.00	40
7L	23	28			Control
	27	108	1.17	4.20	50
8L	17	21			Control
	18	212	1.05	10.0	45
9L	29	35			Control
	14	56	0.45	1.6	65
10L	13	16			Control
	10	Compl. Obstr.	0.77		10
	11	40	0.84	2.5	60
13L	19	24			Control
	22	66	1.05	2.81	45
14L	9.6	11.6			Control
	3.5	10	0.36	0.86	40
	9.7	32	1.01	2.73	50

*Resistance = mean pressure drop across lung (mm. Hg)/flow through lung (L./min.).

blood from the atelectatic lung was the same as mixed venous blood, while that from the normal lung had the same saturation as the arterial blood preoperatively. Throughout the study the animals breathed room air. From these data the per cent of total flow through each lung was calculated, using the same principles as discussed for the acute experiments.

RESULTS

The data obtained from these experiments are listed in Tables I, II, and III. No control values for ratio of flow through each lung were obtained, but previous work[1, 4] has shown that 40 to 45 per cent of the cardiac output in the dog perfuses the left lung. In the acute experiments (Table I), ten to forty-five minutes after bronchial obstruction, the first sampling revealed a reduction in flow through the atelectatic lung to 0 to 34 per cent of the total flow. There was no significant progression when the studies were repeated on the same dog. As a result of this marked reduction of flow through the atelectatic lung, the femoral arterial saturation never fell below 88 per cent. The pulmonary resistance in the oxygen-breathing lung stayed the same or fell, while that in the atelectatic lung increased markedly (Table III).

In the chronic experiments (Table II), flow to the atelectatic lung was reduced to as little as 7 per cent of the total when the first observations were made only two days after operation, and remained essentially unchanged during further observations. The systemic arterial saturation in these chronic experiments was somewhat lower than in the acute ones, ranging from 77 to 92 per cent.

DISCUSSION

The degree of decrease in flow through an atelectatic lung with widely open pleural space and while the animals received artificial respiration was of the same order of magnitude as that found by Moore[1] and Andrus.[2] Since no significant progression was found in ratios of blood flow through the two lungs

after the first study, ten or more minutes after bronchial ligation, this maximal effect may well have occurred as soon as the lung became collapsed. In the animals of the acute series, in which most of the nitrogen was washed out by preliminary bilateral oxygen breathing, complete collapse of the lung was evident within five minutes. A slower progression of atelectasis was observed in the chronic series where room air was breathed through the study.

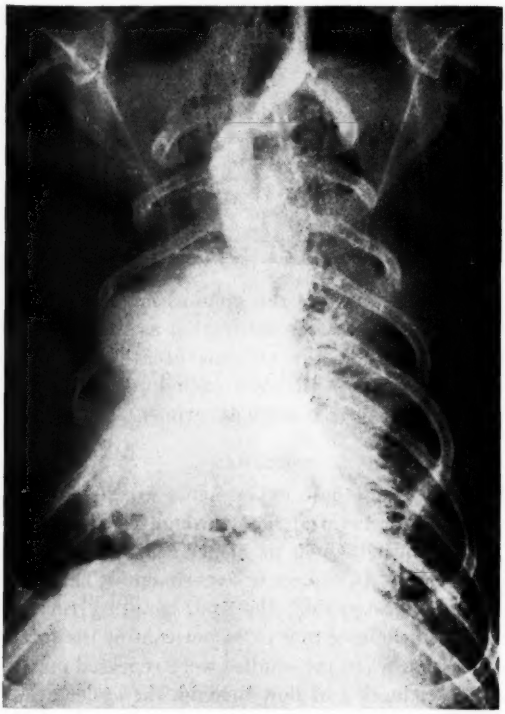

Fig. 2.—Dog No. 16: Intravenous angiogram taken six months after production of atelectasis. Note unchanged diameter of large vessels and failure of filling of small vessels on atelectatic side.

A second difference in the two series was evident from the levels of the arterial oxygen saturation during complete atelectasis. The somewhat higher saturations in the acute experiments were due to the relatively large amount of dissolved oxygen in the blood draining the oxygen-breathing lung. This resulted in an oxygen content of this blood well in excess of the oxygen-carrying capacity of the hemoglobin.

The clinical significance of the magnitude and promptness of reduction of flow following atelectasis is evident. This adjustment prevents a significant drop in arterial saturation when parts of the lung are collapsed during intrathoracic procedures. It is similarly this reduction in flow which enables the arterial oxygen level to be sustained in chronic atelectasis.

It is of interest to point out that reduction in flow due to atelectasis was far greater than that found by us during unilateral nitrogen breathing.[4] This strongly suggests the importance of the mechanical factor (collapse of the lung) in the former. The exact location of the increase in resistance to flow of the atelectatic lung is uncertain. Fig. 2 shows that the large vessels did not appreciably decrease in diameter. The locus must, therefore, be in the small vessels of the lung.

SUMMARY

In two groups of dogs atelectasis of one lung was produced by bronchial ligation. The first group was studied up to three hours after ligation with the pleural space widely opened, under artificial respiration. The flow to the atelectatic lung was reduced to 0 to 34 per cent of the total blood flow due to a marked increase in pulmonary vascular resistance. Maximal effects were observed in the first postatelectatic study, ten to forty-five minutes after ligation.

The second group of dogs was allowed to survive for periods up to six months. Reductions in flow similar to that in the first group were observed.

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DISCUSSION

DR. J. J. FINNERTY, New York.—This work represents an excellent development of the fundamental work of Andrus, Moore, Bergrenn, and Björk. While working with Professor Crafoord, Dr. Carlens and I had an opportunity to make some observations which are pertinent to this work.

Variations in the oxygen saturation of the hemoglobin of peripheral arteriolar blood in fifteen patients undergoing thoracic operations were observed by means of a sensitive oximeter. Adequate ventilation was assured by the use of a mechanical positive pressure anesthesia apparatus, and a double lumened endobronchial anesthesia tube was employed, which permitted inflation or deflation of the lung on the operated side at will.

Upon entering the pleural cavity and disconnecting the lumen of the endobronchial tube going to the operated lung, thus allowing it to collapse, falls in the hemoglobin saturation of the peripheral blood varying up to 40 per cent were noted. This fall was interpreted as being due to the flow of reduced blood through the nonventilated lung, with its consequent return to the peripheral circulation in its original unsaturated condition. This is then, in effect, a pulmonary arteriovenous shunt.

Occlusion of the pulmonary artery to the deflated lung oblitered this "shunt" and, as expected, the peripheral saturation immediately rose to normal or near normal levels. It was further noted that the fall in saturation was roughly inversely proportional to the extent of pathology in the operated lung, being absent or minimal in totally destroyed

lungs, and maximal in well-functioning lungs, as in the case of a small peripheral tumor. This, of course, suggests that as a lung ceases to function, as in atelectasis or suppurative disease, its pulmonary blood flow decreases.

We believe that these observations are clinically significant for the following reasons: first, long periods of collapse of the operated lung that has an intact pulmonary blood flow lead not only to hypoxemia, but probably also to carbon dioxide retention and respiratory acidosis. This can be corrected either by maintaining adequate ventilation to the operated lung, which may make surgery difficult, or by early occlusion of the pulmonary artery to the operated lung. Furthermore, occasionally we see a patient with bilateral emphysema in whom, upon opening the thorax, and permitting the operated lung to deflate, there develops marked respiratory embarrassment and cyanosis, of such a degree as to make us consider abandoning the operative procedure. Early occlusion of the pulmonary artery to the operated lung, closing the "shunt" in many cases results in such marked improvement that the operative procedure may be completed uneventfully.

DR. C. ROLLINS HANLON, St. Louis.—We were interested in this problem several years ago and, in conjunction with Dr. Dean Warren at Johns Hopkins University, we carried out some physiologic studies of the blood flow and other factors associated with atelectatic lungs in dogs. In our experiments the right main bronchus was divided, the proximal end sutured and the distal end left unsutured. We found, as was reported here, that immediately after this procedure there was some depression of the peripheral oxygen saturation of blood. It was usually surprisingly low, in the neighborhood of 55 or 60 per cent. We assumed that that was due to one of two things, either because there was some interference with blood flow to the good lung, due to atelectasis, or because a considerable amount of blood was still going through the atelectatic lung. As time went on, two to six months thereafter, the oxygen saturation of arterial blood gradually rose so that the standard level after two to six months was 88 to 90 per cent, indicating that relatively little blood was running through the atelectatic lung. Therefore we assumed that in the acute stage the unoperated lung was somewhat below par so far as efficiency of oxygenation was concerned. This was confirmed by the finding of patchy atelectasis in the unoperated lung at autopsies which were done electively on dogs one or two days after the operation was carried out.

With regard to pulmonary vascular resistance, we attempted to investigate this by banding the opposite pulmonary artery with reactive Cellophane, so that as months went on one would get constriction of the opposite pulmonary artery driving blood to the atelectatic lung. By this device, which is a useful experimental device for cyanosis (and that is the main reason I mention it) one can achieve, two to six months thereafter, arterial oxygen saturation varying from 65 to 79 per cent as a continuing level.

DR. ROSS ROBERTSON, Vancouver, B. C.—As one who uses endobronchial anesthesia very extensively for pulmonary surgery, I am very grateful to Dr. Peters for his paper. With endobronchial anesthesia, surgery of the lungs is a great deal easier, but we have always been worried as to whether or not the shunt from the atelectatic lung interfered with the oxygenation of the patient. In a few cases we have taken arterial oxygen saturation after the endobronchial catheter was placed, and have found that before the chest was opened there is quite a drop in oxygen saturation of arterial blood. Consequently, in using endobronchial anesthesia, there is some urgency in opening the chest; but as soon as the chest is opened and the lung can collapse, and the vessels collapse with it, the oxygen saturation rapidly rises to approximately 85 to 90 per cent, and so we feel justified in using this type of anesthesia.

DR. PETERS (Closing).—Regarding this marked fall in saturation discussed by Dr. Finnerty, it is important to point out that if animals are given pure oxygen, the amount of dissolved oxygen in a pulmonary vein on the aerated side represents two or three cubic centimeters per 100 c.c. of blood and in this manner the systemic arterial oxygen satura-

tion can be protected even if there is flow through the nonaerated lung. Likewise, the extent of collapse is extremely important. In the experiments in which dogs breathed nitrogen in one lung, the decrease in blood flow was much less than when the lung was collapsed. Thus if the mechanical factor is not utilized, the flow will be greater and therefore the saturation lower. The low saturation might represent poor ventilation of the aerated side.

The oxygen saturation in animals which have 20 per cent of their blood flowing through an atelectatic lung will range, if air is used for breathing, down to 84 or 85 per cent. If the dog is breathing oxygen as in the acute experiments, the oxygen saturation stays at almost a normal level. Our oxygen saturations have been in much the same range as those spoken of by Dr. Hanlon except for the fact that compensation occurred immediately in these experiments and we did not notice any significant further decrease in flow with subsequent observations.

With regard to the use of endobronchial anesthesia, the only suggestion I would make would be to be sure that the patient has all the nitrogen washed out of the lungs and blood by oxygen breathing, so that immediate collapse of the lung will occur following bronchial occlusion.

SURGICAL MANAGEMENT OF PULMONARY EMPHYSEMA

GERALD L. CRENSHAW, M.D. (BY INVITATION), AND
DONALD F. ROWLES, M.D. (BY INVITATION)
OAKLAND, CALIF.

BASED upon the theory that pulmonary emphysema results from bronchospasm and avascularity of the lung with secondary nutrient degeneration, a preliminary report of a new idea in surgical management of pulmonary emphysema is presented. It is felt that the degenerative cycle of pulmonary emphysema may be interrupted by establishing collateral circulation to the lung.

From a physiologic and pathologic standpoint, pulmonary emphysema is divided into four categories: (1) diffuse hypertrophic emphysema; (2) subpleural bullae and blebs; (3) localized degeneration, more commonly known as "cotton-candy lung"; and (4) a combination of two or three of these conditions.

The etiology of pulmonary emphysema has been variously attributed to chronic cough, loss of elasticity, recurrent bronchial infection, bronchospasm, and occupational hazards, or has been considered as secondary to chest wall changes.[6, 11] However, pathologically the bronchial arteries may show arteriosclerotic and endarteritic changes which may produce loss of elasticity with thinning of the alveolar walls and degeneration. Thus there is a resultant diminution of the capillary bed of the lung,[13] although there is some difference of opinion on this latter point.[2]

In spite of marked pressure differentials in the systemic and pulmonary vessels, it is well known that, in the normal lung, there is free communication between the two systems through the subpleural capillaries. In the diseased lung, it has been demonstrated, pathologically and experimentally, that there are blood shunts which allow free flow from the diseased tissue into functioning alveoli.[15, 16, 17, 22] These blood shunts are physiologically similar to air drifts.[7, 20, 21] They develop between the systemic and pulmonary systems wherever infection in a lymph follicle takes place, and have been demonstrated to exist freely in bronchiectasis, pulmonary emphysema, and congenital pulmonary atresia.[12] Secondary to infectious processes, these vascular shunts occur near the termination of cartilaginous bronchi.

In animal experiments, by varying pressure differentials in systemic and pulmonary arteries, systemic blood has been demonstrated beyond the pulmonary capillaries. If the pressure is high enough or maintained long enough, systemic blood can be demonstrated, by catheterization studies, to be present in major segmental pulmonary arteries. This retrograde flow of systemic blood would then be shunted into other pulmonary radicles. In dogs the systemic to pulmonary

Read at the Thirty-Second Annual Meeting of The American Association for Thoracic Surgery at Dallas, Texas, May 8-10, 1952.

shunt has been shown volumetrically to be one-third greater than the normal output of the left ventricle.[12] Study of increased pressure within the pulmonary artery has shown retrograde flow as far as the aorta.[10]

It has long been established that a collateral blood supply, by way of the intercostals, enters the lung through vascularized adhesions. For this reason, in doing intrapleural pneumonolysis for tuberculosis, the procedure is done within a period of two months from the onset of collapse so that troublesome bleeding from vascularized adhesions can be avoided. It has been noted, in tuberculous patients in whom emphysema might be expected, that under areas of pleural symphysis and vascularized adhesions emphysema actually does not occur.[14] This is contrary to what would be expected with the proliferative changes in the blood vessels and bronchostenosis in tuberculous lungs.

In certain cases of pulmonary atresia, life has been maintained by the ingrowth of collaterals from the intercostal, internal mammary, pericardiophrenic and esophageal vessels.[4, 5, 19] These new collaterals communicate with the pulmonary artery radicles, through shunts and through the alveolar capillaries. In fact, thoracotomies with pleurectomies have been performed to establish such new collaterals.[5]

It has been demonstrated in animal experiments that prolonged bronchial obstruction produces irreversible emphysema. Chronic partial bronchial obstruction, either by bronchospasm or secretions, is felt to be an important factor in clinical emphysema. Certain clinical cases of emphysema have benefited by complete denervation (sympathetic and parasympathetic), which reduces the factor of bronchospasm.[1]

The benefit derived from the surgical removal of space consuming bullae and blebs has been pointed out.[9] In our opinion, this is equally true of atrophic lung.

OPERATIVE TECHNIQUE AND MATERIAL

The above ideas are incorporated in a surgical approach to the treatment of pulmonary emphysema. An open thoracotomy is done. Degenerated lung is removed by segmental resection or lobectomy. Subpleural bullae and blebs are removed by clamp resection. Smaller bullae and blebs are treated by individual mattress sutures. As far as possible, all air leaks are controlled. Complete vagal denervation is accomplished by severance of branches at the hilum, including those from the left recurrent laryngeal nerve. Perivascular and peribronchial tissues are dissected and the inferior pulmonary ligament is severed (Blades' technique[3]). The sympathetic chain is removed from the third through the ninth ganglion, including the splanchnic nerves. The parietal pleura is removed from the chest wall. Irritative sterile talc is powdered over the visceral pleura. When the chest is closed, two large intercostal tubes are inserted to which regulated suction is applied as soon as the patient is returned to his room.

Eleven cases of pulmonary emphysema have been so surgically managed (Table I). Ten cases have had unilateral procedures, and in one case excision of bullous disease on the opposite side had been done three years prior to the present surgery.

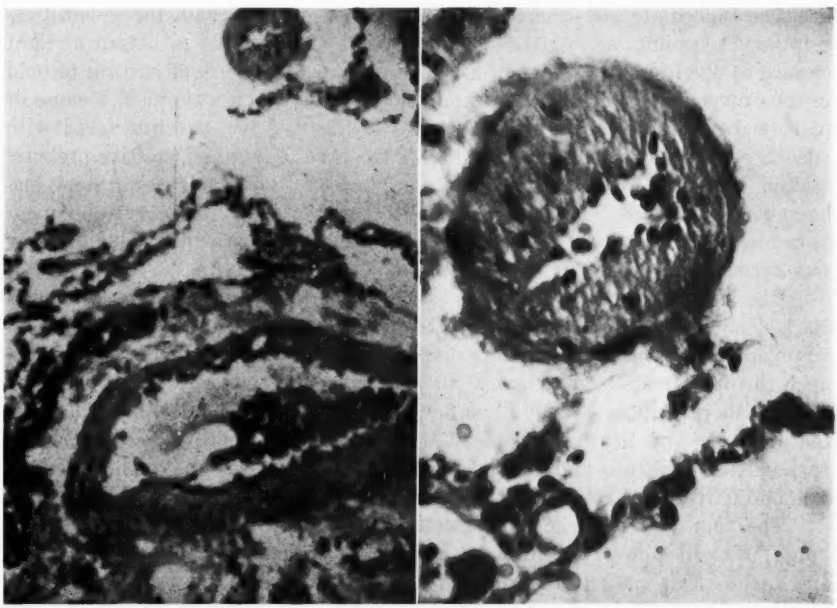
TABLE I. CLINICAL RÉSUMÉ OF 11 CASES OF PULMONARY EMPHYSEMA SURGICALLY MANAGED

NAME	AGE	SEX	SYMPTOMS	IMMEDIATE PREOPERATIVE STATUS	ROENTGENOGRAM DIAGNOSIS	GROSS PATHOLOGY OF SURGICAL SPECIMEN	TIME OF FOLLOW-UP AFTER SURGERY	CLINICAL STATUS AT LATEST DATE OF FOLLOW-UP
B. G.	66	M	Dyspnea; orthopnea; cyanosis, mild	Condition critical	Diffuse pulmonary emphysema, bilateral; compression atelectasis, bilateral	None	24 mo.	Full-time activity; dyspnea only on extreme exertion; lies flat for sleeping
F. K.	48	M	Marked dyspnea; orthopnea; cyanosis, marked	Condition critical	Diffuse pulmonary emphysema, bilateral	None	15 mo.	Working 8 hr. day as counterman in lunch room; mild dyspnea on exertion; no cyanosis; lies flat for sleeping
T. H.	59	M	Marked dyspnea; orthopnea; cyanosis, mod.	Condition critical	Bullous emphysema, bilateral	Degenerated lung, lobar and segmental	14 mo.	Working full time, managing lumber yard; mild dyspnea on extreme exertion; lies flat for sleeping
D. M.	38	F	Asthma; dyspnea, mod.; orthopnea	Activity markedly restricted	Diffuse pulmonary emphysema, bilateral	None	10 mo.	Has resumed full household duties; mild dyspnea on extreme exertion; asthma continues
R. F.	65	M	Dyspnea	Ambulatory but activity becoming more restricted	Bullous emphysema, bilateral	Bullous emphysema; chronic pleuritis	8 mo.	Full-time activity; mild dyspnea only on extreme exertion
J. Y.	60	M	Marked dyspnea; orthopnea; cyanosis, marked	Bedridden, under oxygen therapy	Bullous emphysema, bilateral	Degenerated lung, lobar and segmental	6 mo.	Has returned to full-time heavy labor, driving logging truck; lies flat for sleeping
A. R.	75	M	Marked dyspnea; orthopnea; cyanosis, mod.	Activity markedly restricted	Bullous emphysema, bilateral	Bullous emphysema; degenerated lung, lobar and segmental; pleural fibrosis	4 mo.	Able to walk 2 blocks; drives his car regularly on 20-mile trips; lies flat for sleeping
M. T.*	47	M	Marked dyspnea; orthopnea; cyanosis, marked	Condition critical	Bullous emphysema, bilateral	Bullous emphysema	2 mo.	Still hospitalized; general condition improved
M. S.	43	M	None; disease revealed on routine roentgenogram	No disability	Bullous emphysema, bilateral	Bullous emphysema	6 wk.	Working full time as office clerk
M. D.	48	M	Productive cough; wheezing; dyspnea on exertion	Activity becoming more restricted, but able to work	Bronchiectasis left lower lobe	Bronchiectasis, left lower lobe; bullous emphysema; degenerated lung, left upper lobe	5 wk.	Working full time as hospital porter
J. W.	65	M	Marked dyspnea; orthopnea; cyanosis, marked	Completely bedridden, under oxygen therapy	Bullous emphysema, bilateral; silicosis, bilateral	Bullous emphysema; silicosis	13 days	Dead. Death due to persistent air leaks

*This patient's surgery was three years after removal of extensive bullae from the opposite lung (right).

Three cases were of the diffuse hypertrophic type; 2 of the "cotton-candy" type; 4 cases had bullous disease alone; and 2 cases had bullous disease with "cotton-candy lung."

The advantages of removing space consuming lesions and allowing more lung to become functional was an obvious indication for surgery. Denervation was done because of the successful experience of other surgeons in reducing bronchospasm. Parietal pleurectomy was accomplished so that the lung would become adherent to the chest wall. The ingrowth of systemic collaterals into the pulmonary tissue possibly stopped the further development of emphysema. No autopsy material is available to substantiate this point. In the cases recently operated upon poudrage has been done to enhance the pleural chest wall symphysis.



A. *B.*

Fig. 1.—*A*, Microsopic section of pulmonary emphysematous lung showing loss of alveoli and chronic bronchitis with peribronchial inflammatory changes. An associated artery is shown at the top. (× 100.) *B*, Enlargement of the artery seen in *A*, showing advanced medial and intimal thickening. (× 400.)

Pathologically, the surgical specimens show the typical changes of emphysema. Advanced bronchial endarteritis is demonstrated (Figs. 1, *A* and 1, *B*). Chronic peribronchial inflammatory infiltrations are usual and frequently bronchial wall degeneration is seen.

RESULTS

Most of the patients were complete respiratory cripples in whom a medical regimen of bronchodilator drugs, oxygen, antibiotics, bronchial drainage, pneu-

moperitoneum, abdominal belts, and treatment of any concurrent cor pulmonale had failed to influence the progression of the disease. In the face of advanced emphysema progressing under medical management, surgical intervention was tried. With more experience, surgery was found to be indicated particularly in those patients with degenerative ("cotton-candy lung") and bullous disease.

These patients were poor risks for surgery. All were dyspneic, and some orthopneic and cyanotic. However, with the introduction of positive pressure anesthesia, their general condition moderately improved and they tolerated the operation surprisingly well. In those patients with bullous disease, as soon as the thoracic cavity was opened there was immediate improvement in their ventilation and course, as compression of the lung was relieved by the protrusion of the bullae into the wound, and this improvement continued after surgical removal of the bullae.

The immediate postoperative period in those patients with the greatest respiratory crippling was extremely stormy. It was difficult to obtain airtight closure of the lung at surgery in all cases, because of failure of sutures to hold in lung of poor tensile strength. Limitation of respiratory excursion, because of pain, embarrassed their low pulmonary reserve, and likewise interfered with adequate tussive removal of secretions. Two patients required positive pressure oxygen therapy (Bennett valve) temporarily to relieve their respiratory embarrassment. After clearing of the tracheobronchial tree at surgery subsequent bronchoscopies were not required. Early ambulation without oxygen therapy was encouraged.

The late postoperative course of three patients with bullous disease showed marked improvement. Two returned to full-time work within three months after operation. One patient with extensive bilateral bullous disease, who developed cardiac arrest on induction of anesthesia, has been followed for a period of two months postoperatively. He is now semiambulatory, but is still confined to the hospital. One death occurred, at thirteen days after operation, in a patient with extensive silicosis and bullous emphysema. Death was due to persistent air leak and partial lung collapse with ultimate respiratory failure.

The four patients who had resection of degenerated lung ("cotton-candy lung") showed slower improvement than those patients with subpleural bullae and blebs. One patient returned to limited work within seven months after operation, and within one year was doing full-time work, managing his own lumber yard. Another of these patients returned to full-time heavy labor, driving a logging truck, within four months after operation. The late postoperative course of a third patient in this group is described in Case 2. The fourth patient in this group has just returned to full-time work, as a hospital porter, after five weeks' postoperative convalescence.

The three patients with diffuse hypertrophic changes required three to four months before slow improvement was noted. One patient was able to reume her usual household duties within a period of six months after operation. Attacks of asthma following an upper respiratory infection caused a return of marked dyspnea and cyanosis, but this subsided with clearing of the infection and she is again doing all her housework. Another patient was working eight hours a day, as counterman in a lunch room, within six months after operation, and has

continued at this work with only one interruption of two weeks' duration because of a severe bronchial infection, which cleared promptly under antibiotic therapy. The late postoperative course of the third patient is described in Case 1.

CASE REPORTS

CASE 1.—B. G., a 64-year-old white man, was first seen by us in Peralta Hospital on June 15, 1948. The referring physician desired bronchoscopy because of difficulty in breathing secondary to an acute bronchial infection. The patient, a retired manufacturer, had recently been sent to California from the east coast because of asthma and progressive dyspnea. Bronchoscopy revealed bilateral thick sputum. There was generalized edema and reddening of the tracheobronchial mucosa.

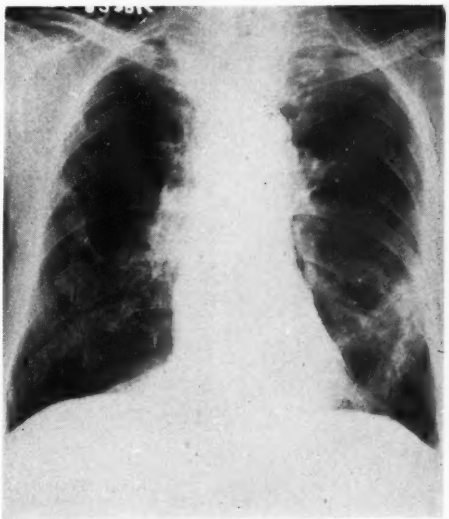


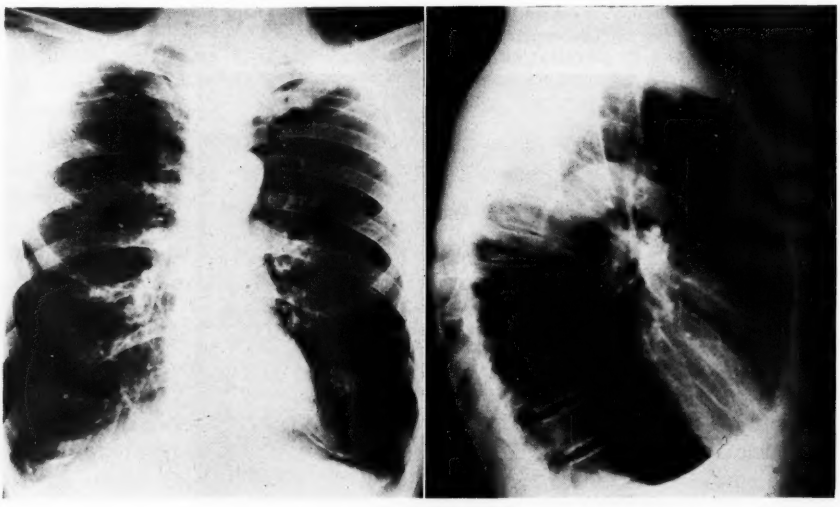
Fig. 2.—(Case B. G.), April 7, 1952. Postoperative roentgenogram showing narrowing of left intercostal spaces.

The medical management of this patient consisted of the following: His smoking was completely restricted. He was placed on a salt-free diet, on breathing exercises, and on Aerosol and intramuscular antibiotics. He was given mercurial diuretics for cor pulmonale. Under this medical management he temporarily improved, but again progressive dyspnea and orthopnea were noted. Finally, in May, 1950, hospitalization was required because of exacerbation of these symptoms, and he failed to respond to diuretics, antibiotics, or to continuous oxygen therapy. Surgical management by denervation and resection of bullae had been reported, and the idea of pleurectomy, with development of collateral circulation, occurred to us. With the failure of medical management in this case, surgical intervention was thought worth trying.

Physical examination just prior to surgery revealed a dyspneic, orthopneic, and mildly cyanotic man, whose condition was critical. Pertinent findings were an emphysematous chest with suppression of breath sounds and prolonged expiration through pursed lips. Scattered râles and rhonchi were heard at both bases.

Laboratory work revealed a polycythemia of 6,200,000 red blood cells, and a hemoglobin of 110 per cent. A chest roentgenogram showed typical findings of generalized diffuse hypertrophic emphysema.

On May 12, 1950, a left open thoracotomy was performed, under positive pressure anesthesia which the patient tolerated surprisingly well. A diffuse type of emphysema, without bullae or bleb formation, was found. The pulmonary artery was markedly enlarged. Blades' technique of vagal denervation to the lung, removal of sympathetic dorsal ganglion chain, severance of inferior pulmonary ligament, and perivascular and peribronchial dissection was carried out. The parietal pleura was removed from the chest wall, but not from the mediastinum and diaphragm. The chest was closed with two intercostal drainage tubes, to which regulated suction was applied as soon as the patient was returned to his room.



A. *B.*

Fig. 3.—*A* and *B* (Case A. R.), Dec. 17, 1951. Posteroanterior and right lateral roentgenograms showing pulmonary emphysema with bullous formation at right top.

The postoperative course was stormy, due to ineffectual cough and poor respiratory reserve. Minimal pleural fluid absorbed within a few days. Within two months after operation the patient became ambulatory, and has continued to improve slowly. His blood count is normal. He now makes routine trips across the continent, and is dyspneic only on extreme exertion, consistent with his age. He was recently hospitalized for bilateral virus pneumonia, from which he made an uneventful recovery.

It is interesting to note that this patient has had episodes of bronchial wheezing during asthmatic attacks as marked on the denervated side as on the opposite side. However, physical examination usually reveals a free passage of air in the bronchial tree of the operated side, while on the opposite side multiple rhonchi and râles frequently can be heard. There has been an obvious decrease in the circumference of the operated side of the chest, and roentgenograms now reveal a decided narrowing of the intercostal spaces (Fig. 2).

CASE 2.—A. R., a 73-year-old white male machinist, was referred to us by his attending physician on May 22, 1950, because of progressive dyspnea and weakness. He was unable to stand for longer than ten minutes, and could not walk more than 30 feet without becoming markedly short of breath. He had been well until 1945, when he began to develop the above symptoms following a severe cold.

Physical examination revealed a markedly dyspneic man, appearing much younger than his stated age. Pertinent findings were limited to an emphysematous chest, with diminished breath sounds throughout.

Laboratory work revealed a normal blood count and urinalysis. Chest roentgenograms showed bilateral emphysema with bullae at the right apex. An electrocardiogram was normal.

The following medical therapy was instituted: The patient's smoking was completely restricted. He was placed on heliotherapy, bronchial expectorants, and carbogen therapy. He was given mercurial diuretics for cor pulmonale. Under this regimen his symptoms were relieved temporarily. However, his general condition gradually grew worse, to the point of complete invalidism from further dyspnea and weakness, and surgery was deemed necessary (Figs. 3, *A* and 3, *B*).

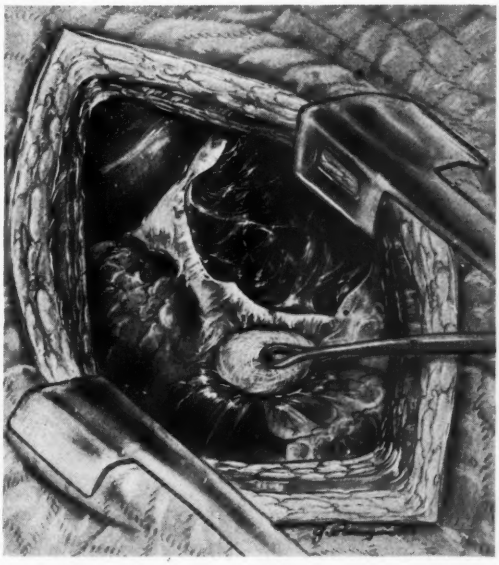


Fig. 4.—Degenerated lung ("cotton-candy lung").

On Jan. 8, 1952, a right open thoracotomy was performed at Samuel Merritt Hospital, under positive pressure anesthesia. The entire upper lobe and the superior segment of the lower lobe were found to be degenerated ("cotton-candy lung") (Fig. 4). The remainder of the lung showed diffuse hypertrophic emphysema. A lobectomy, segmental lobectomy, and complete denervation were done. The parietal pleura was removed from the chest wall, and air leaks from raw surfaces were controlled as far as possible. Irritative sterile talc was powdered over the visceral pleura, and the chest was closed with two drainage tubes, to which regulated suction was applied as soon as the patient was returned to his room.

The postoperative course was stormy due to mild respiratory embarrassment and persistent air leaks of six days' duration. Localized fluid formed and required one aspiration. On the eighth postoperative day the patient became ambulatory, and was discharged home on the fourteenth hospital day.

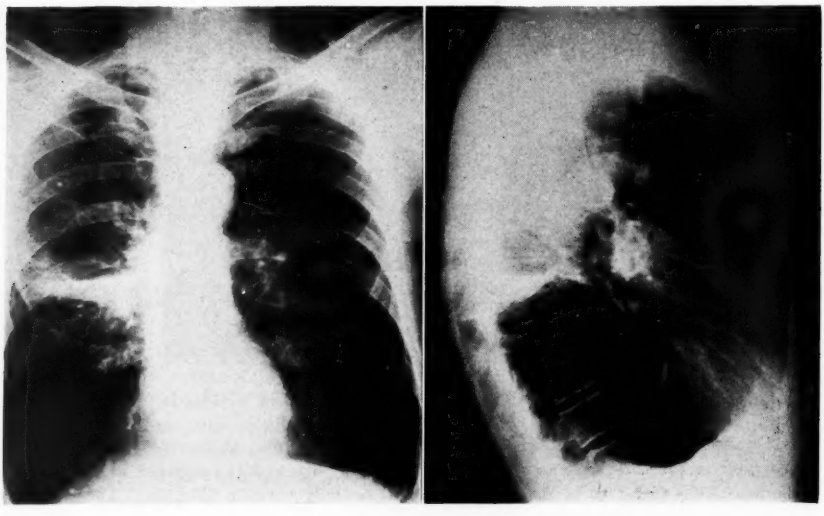
He has showed slow but steady improvement (Figs. 5, *A* and 5, *B*), and is now able to walk two blocks and drives his car twenty miles without difficulty.

Pulmonary ventilatory studies, including cardiac catheterization, were done preoperatively and at three months postoperatively. Comparison of the findings of the two studies reveals no significant changes. Subsequent studies are planned.

SUMMARY AND CONCLUSIONS

Various aspects of pulmonary emphysema are discussed, and the rationale of the surgical approach to treatment is given. The object of the surgery is to allow more lung to become functional, to reduce bronchospasm, and to supply the remaining lung with collateral circulation. The manner by which this systemic collateral circulation reaches the pulmonary capillaries is described.

Eleven patients with advanced pulmonary emphysema, including the three types of diffuse hypertrophic, subpleural bullae and blebs, and degenerated lung, have been surgically managed by removal, from one lung, of degenerative and bullous disease, complete denervation, and parietal pleurectomy. Degenerated lung was found to be lobar or segmental in distribution. In all instances, the pathologic study of the surgical specimens revealed advanced changes in the blood vessels and in the bronchi.



A. *B.*

Fig. 5.—*A* and *B* (Case A. R.), April 8, 1952. Posteroanterior and right lateral roentgenogram showing pleural symphysis, right, with localized pleural fluid collection.

Although, in the main, the patients in this series were severe respiratory cripples, they tolerated the surgery well. One death occurred thirteen days postoperatively due to persistent air leaks. The immediate benefit in these patients was undoubtedly due to the denervation and removal of space-consuming lesions, but their continued improvement must be attributed to the ingrowth of collateral circulation.

TABLE II. RESULTS OF PULMONARY FUNCTION STUDIES

	PREOPERATIVE	POSTOPERATIVE (3 MO.)
Cardiac output	3.5 L./min.	
Heart rate	110	110
Stroke volume	32 c.c.	
Minute volume	7.24 liters	6.8 liters
Tidal air	575 c.c.	600 c.c.
Arterial saturation	90 per cent	89 per cent
R. Q.	0.92 per cent	
Pulmonary artery pressure	37/21	
pH	7.42	7.42

The previous treatment of pulmonary emphysema has been able only to prolong its inevitable cycle. From our observations in the present series of patients it is felt that the degenerative cycle of pulmonary emphysema may be interrupted by establishing systemic collateral circulation to the lung. The clinical improvement in these patients warrants further trial of this procedure.

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DISCUSSION

DR. OSLER ABBOTT, Atlanta, Ga.—I want to congratulate Dr. Crenshaw on his work. This has been our major investigative problem on the Chest Service at Emory University School of Medicine since 1945. We were able to present in Boston this month the results of studies on over 300 patients with pulmonary emphysema, an operative intervention register of 125, with follow-up studies both clinical and physiologic.

I would like to trace a little of the history of the operative procedure we have utilized for emphysema. First, we have not purposely used the parietal pleural stripping procedure for Stage V patients. We are certainly going to give it a try, but without preponderance, and we are very grateful for that additional concept. We have used it on tetralogy of Fallot and have had beneficial results in three patients. The origin of our application of the idea was in an operating room-locker room conversation in 1946, between Dr. Willis Potts, Mr. Brock, and myself. They commented upon the work of a French surgeon who had suggested that parietal pleural excision should be beneficial and should be done on the next tetralogy that presented no pulmonary arteries. The discussion included a considerable amount of reference to a conversation between Dr. Potts and Dr. Blalock in which they both were of the opinion that this might be a valuable procedure. This is the historical background so far as I know, of this part of the problem. So far as I know, the plan of combining an upper dorsal sympathectomy with parietal pleural stripping was original with us in 1946. Our patients on whom this procedure was successful have had a marked decrease in cyanosis, full cessation of squatting, and activity potential has approached normal limits.

The next part of the problem was in 1945 when we did our first total complete plexectomy on a patient with cor pulmonale, with benefit. He died in three years and this discouraged us. Brian Blades awakened our interest again by describing complete plexectomy. Dr. Samson made a major contribution in regard to the bullous aspect of the disease. At the 1949 meeting of this Association we presented the proposition that denervation procedures, plus excisional surgery, were indicated in pulmonary emphysema. We have now come to the point that we feel as follows: there are two fundamental types of disease in medicine. This is the disease which is due to a single etiologic agent, such as pneumococcal pneumonia. Then, there is another concept which we derived from a luncheon meeting of Dr. Graham's residents two years ago, namely, that there is a synergism, a combination of factors involving varying agents, which goes to produce more complicated medical disease syndromes. A subdivision of this group is, that in some of these diseases the early local organic damage resultant to the disease becomes an additional factor in the progression of the disease. This is the philosophy and the fact, and a greater appreciation of this should aid in the approach to this problem and other chronic atrophic disease. I would like to present a couple of slides:

(Slide.) This part of the study is where patients were evaluated with regard to the degree of bronchospasm present in the emphysematous individual. Only 85 per cent of our series of 250 had demonstrable bronchospasm by our present methods. This is one of the types of measurement of maximum breathing capacity before and after the injection of many different drugs. Usually these tests are described by the patient when he tells you which drug is most effective.

(Slide.) This represents an improved technique for transacting emphysematous lung tissue which we devised because we had tragic experiences in 1946 and 1947 of patients with diffuse hypertrophic emphysema, dying because of interstitial hemorrhage or hemorrhagic pneumonitis arising from the course of the suture line. The principle that we should suture through nonflowing blood is applied here. The Potts' coarctation clamp

(multitoothed) is applied over the tissue that will remain as the suture line. Interrupted silk sutures are placed distal to the clamp and reinforced by a running suture of fine atraumatic catgut. Thus, the air leaks, to which Dr. Crenshaw referred, are eradicated.

(Slide.) Dr. Van Fleit, who is associated with us at Emory, had the courage to safely attempt to carry out an angiocardiogram, by a method which we had devised, in the extremely sick individual. These are patients whose maximum breathing capacity may be as low as 13, 15, 18, 20. Applying special antibronchospastic measures allowed us to go ahead and carry out angiocardiograms in the severely ill emphysematous patient before and after surgery. Steinberg, in 1942, had a beautiful demonstration of 27 non-operative pulmonary emphysema angiocardiograms. Both of these studies emphasize one of the pathogenetic characteristics of the disease, namely, that this is originally a local disease. When we teach the general practitioner to attend pulmonary emphysema in its stage of primary local character, and often the patient only says, "doctor, I get shorter of breath than my brother . . . ,"—then we should have opportunity for full cure of these patients. Here is the local character of the disease. This is a postoperative angiocardiogram. Here is the upper lobe area.

(Slide.) This represents the preoperative film. This potentially functioning lung shows at the left base, hypertrophic emphysema, and I am fascinated to see that we have the same pattern in these arteries that Dr. Peters showed with the obstruction in the bronchus. The postoperative film shows refunctionalization of a previously compressed and defunctionalized lung.

(Slide.) These show the various types of emphysema which may be cured or palliated. The premise, therefore, is that all types and combinations of pulmonary emphysema are potentially curable in their earlier stages. Certainly we have shown that major palliation is possible even in the fifth, or last stage of the disease.

DR. MAX G. CARTER, New Haven, Conn.—If I may be permitted, I should like first to congratulate Dr. Crenshaw for his interest in emphysema, because I think this is one of the single most important pulmonary diseases which we see. Second, I should like to be allowed the temerity to take issue with his logic. We have been concerned with emphysema for several years and the more we study it the less we know about it. But it does seem to me that definitions are of great importance. When one speaks of hypertrophic pulmonary emphysema, he must exclude asthma or bronchospasm, and that can be excluded in the laboratory, of course. Although the characteristic hypertrophic emphysema may follow a long course of asthma, certainly we must distinguish the surgical objectives. Is the operation aimed at asthma by nerve-cutting methods or is it aimed at emphysema which, by definition, is not asthma? Second, there is the problem of pulmonary cysts. It is true that diffuse bullae and blebs are present in many patients with emphysema, but there are other causes for pulmonary cysts as well. These may impair function by expansion of their own size, thereby compressing adjacent pulmonary tissue and interfering with ventilation. Third, is the type of emphysema you see in inflammatory states—commonly, patients with fibrotic contracted fibrotic tuberculous lobes will have overdistention of adjacent lobes and that, to be sure, is emphysema. But certainly etiologically and pathologically it must be distinguished from those patients with bronchiolar obstruction and long-standing so-called hypertrophic emphysema.

Now, what is this hypertrophic emphysema? Long ago Drs. Amberson and Spain described bronchiolar obstruction of a hyaline nature in patients with this far-advanced disease, which is diffuse, so that all lobes are symmetrically enlarged. Late in the disease there may be isolated blebs and bullae. We have found, as have others, that these patients, who may have reduced ventilatory function to the point of a maximum breathing capacity of perhaps 20 or even 12 liters per minute, will have an apparently increased bronchospastic element. That is to say, a drop of 10 liters due to bronchospasm is more important to you when you have a maximum function of only 25. I am impressed by the fact that this is truly, therefore, ventilatory impairment. The problem with these patients is that they cannot get enough air in and out of their lungs. A secondary problem is the

increased residual air, which means that every breath that comes in is diluted in a large volume, much greater than the normal. In other words, residual air in the normal is approximately 20 per cent of full lung volume and, in emphysema patients, it may become as large as 50 or 60 per cent of total lung volume. There is, therefore, retention of carbon dioxide and there may actually be a change in the blood pH in advanced cases. Conversely, the oxygen tension at the alveolo-capillary membrane is markedly reduced.

If it is not possible for an individual to get enough air in and out of his lungs, you do not make him any better by bringing more blood to his lungs. And these patients are therefore not comparable to the tetralogies or other blue cardiacs because in those cases there is ample air in and out of the lung but there is not adequate blood, or at least the blood is not going in the right place.

The reasoning therefore seems to me fallacious that one can improve emphysema patients of the hypertrophic type by pleural poudrage.

The last point I would like to make is that almost regardless of what you do for these chronic invalids, if you do it carefully, with tender loving devotion, they get temporarily better. If you put them in a hospital and increase their bronchial drainage with ammonium chloride, if you give them a few whiffs of oxygen with a pressure apparatus, if you give them a large volume of antibiotics, they will be improved; and one must exclude that improvement from the improvement specifically related to the surgical operation. Dr. Whittenberger and others have demonstrated that if you put such a patient in a respirator so that his residual volume is reduced to normal mechanically, a few hours a day for a week or so, he will have improvement, some of which remains even for a year. We have shown similarly, that if we give these patients pneumoperitoneum and if it is efficient, functionally effective and tolerated well, it may be maintained for perhaps six months and then abandoned and the patient will maintain a certain percentage of that improvement for up to two years. I would like to suggest, therefore, in summary, that the improvement which is being attributed to the increased vascularity of the lung is, in effect, due to a combination of many factors; some of which may partially reduce the residual air, some of which improve the bronchial toilet, diminish the secretions and make the ventilatory function of the lung somewhat more effective.

DR. CRENSHAW (Closing).—I anticipated Dr. Carter's criticism and, in answer, I would like to reiterate that it is our feeling that bronchospasm undoubtedly plays a large part in the production of all three types of emphysema, but it is hard for me to conceive that bronchospasm alone can cause such massive destruction of a lobe or segment as seen in these pictures.

Before reporting our theory and procedure we have waited for an observation period of approximately two years on some of our patients. I would like to call attention to the fact that the patient followed for the longest period of time had failed to respond to a medical regimen, as outlined by Dr. Carter, and therefore surgery was decided upon. This patient was of the diffuse hypertrophic type. Since surgery he has required no medical regimen for the emphysema. He recently went through an attack of bilateral virus pneumonia with rapid recovery. He is now able to make trips across the continent and leads a normal life for a man 67 years of age.

I want to thank both Dr. Abbott and Dr. Carter for their comments.

OBSTRUCTIVE PNEUMONITIS SECONDARY TO BRONCHIAL ADENOMA

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BRONCHIAL adenoma is usually a slow-growing tumor which metastasizes in about 5 to 10 per cent of cases but which, by bronchial occlusion and its effects, often does its most serious harm to the patient. This latter aspect of these tumors has been often mentioned in the literature and is familiar to those who deal with such problems. However, several questions arise in regard to suppurative disease associated with adenoma. Such questions as to frequency, form, and effect on resectability, morbidity, and mortality are those to which an exact answer based on a large experience is not sufficiently emphasized in the literature. This study was undertaken in an attempt to answer some of these questions and to emphasize other known facts.

HISTORICAL

In Mueller's[1] case in 1882, which was the first case of bronchial adenoma described, many bronchiectatic cavities distal to the tumor were found at necropsy. In Heine's[2] case in 1927, bronchiectasis also was distal to the tumor.

Reisner,[3] in 1928, reported a case in which death was due to putrid empyema, and an obstructing bronchial adenoma was found at necropsy. Kramer,[4] in 1930, reported two cases in which multiple attacks of pneumonia and pleurisy occurred. Wessler and Rabin,[5] in 1932, reported seventeen cases of benign bronchial tumors, twelve of which were adenomas. From a study of the reports of these cases, it seems apparent that in at least eight of these twelve there was evidence of moderate to severe obstructive pneumonitis.

Foster-Carter,[6] in analyzing the clinical features of all cases reported up to 1941, including twenty-two of his own, found that in 38 per cent of all cases there was clinical evidence of pleurisy and pneumonia, in 15 per cent there was bronchiectasis, in 7 per cent there was empyema, and in 2 per cent there was pulmonary abscess. Foster-Carter also analyzed the causes of deaths in his and prior cases, and found that of the seventeen deaths six were due to empyema and pulmonary abscess, one was due to pneumonia, three were due to hemoptysis, three followed thoracotomy, and four were due to unrelated disease. He further stated that eventually in 60 per cent of cases bronchiectasis, pulmonary abscess, or empyema will develop. Mallory[7] stated that one must expect bronchial plugging with obstruction and destruction of pulmonary tissue in almost every case in which treatment is not given.

Received for publication March 2, 1952.
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Brunn and Goldman[8] pointed out that occurrence of a lesion of the central nervous system in a case of long-standing adenoma is almost always the result of metastatic septic emboli from the associated pulmonary suppuration. They also stated that in cases of bronchogenic carcinoma episodes of pulmonary suppuration are usually continuous and progressive, and in cases of adenoma they are intermittent, and when death occurs in adenoma it is usually a result of suppurative disease.

Adams, Steiner, and Bloch,[9] in reporting on five cases in 1942, found evidence of metastasis of malignant tissue in three of the five. However, in three of the four deaths in the five cases, suppurative pulmonary disease was the cause of death or was a major contributing factor, and in none was metastasis of malignant tissue or carcinomatosis a cause of death.

Clerf and Bucher[10] found suppurative disease or atelectasis in 60 per cent of their cases. They stated that endoscopic removal of the endobronchial portion of the tumor will relieve to a large extent the suppuration, but the bronchiectasis persists. Jackson, Konzelmann, and Norris[11] stated that endoscopic drainage at least is always advisable in such cases. Holley[12] found chronic pneumonitis in eighteen of thirty-nine cases and "suppuration in only a few." Van Hazel, Holinger, and Jensik[13] had one case in their series in which pleural reaction and suppuration made it impossible to perform resection.

Goldman and Conner[14] found significant severe pulmonary suppuration in ten of thirty-eight cases. This was the direct cause of death in two cases in which embolic brain abscesses were present. Septic cerebral emboli occurred in another case. Two of their patients were treated by preliminary drainage (rib resection) before pulmonary resection was attempted.

Delarue[15] compared the postoperative morbidity in eleven cases of bronchial adenoma in which pneumonectomy was performed with a comparable group of bronchogenic carcinoma and found 45.4 per cent morbidity in the adenoma cases compared with 24.1 per cent morbidity in the cases of carcinoma. His belief was that this was due to the associated suppurative disease found with bronchial adenoma.

RESULTS OF THE STUDY

This study is of the 102* cases of bronchial adenoma encountered at the Mayo Clinic through December, 1950. This includes both the carcinoid and cylindroma types, and excludes any similar neoplasms of the trachea. The tissue was reviewed in all cases so that no errors in pathologic diagnosis would be included. Eighty-six of these cases have previously been reported by Moersch and McDonald,[16] and some of the present data merely supplement their work.

Age.—The average age was 42 years. The oldest patient was aged 70 years, the youngest 15 years. The majority of patients were in the 30-through-49-year age groups.

Sex.—There were fifty-five males and forty-seven females.

Duration of Symptoms.—Six patients were completely asymptomatic. Twelve patients had symptoms of nine years' duration or more (two of whom

*This group does not include an additional four cases in which the histologic pattern was not absolutely typical of adenoma, but which probably represent metastasizing adenomas. These cases, plus others, form the basis for a separate report.

had had symptoms for thirty-six years). Excluding these twelve long exceptions, the average duration was twenty-nine months. Including the long exceptions, the average duration was fifty-four months.

Symptoms.—In decreasing order of frequency the more frequent symptoms were: (1) cough, (2) hemoptysis, (3) recurrent episodes of pneumonitis, (4) thoracic pain, (5) fever, (6) dyspnea.

Physical Examination.—In decreasing order of frequency the more frequent findings were: (1) decreased breath sounds over involved area, (2) dullness over affected area, (3) negative thoracic findings (twenty-six cases), (4) lag of thoracic movement on breathing, and (5) râles over affected area. In three cases a diagnosis of postpneumonic empyema had been made before the patient came to the clinic, and rib resection drainage had been done in two of them.

Roentgenographic Findings.—Findings in decreasing order of frequency were: (1) segmental consolidation or atelectasis, (2) peripheral mass (often well circumscribed), (3) hilar mass, (4) evidence of bronchiectasis, (5) negative thoracic roentgenogram (ten cases).

Bronchoscopy.—Results of bronchoscopic examination were: (1) negative in eight cases (seven of these peripheral location), (2) not done in four cases (peripheral location), (3) positive in 92 per cent of those examined or 88 per cent of total group.*

Treatment.—The 102 cases may be divided into two groups from the standpoint of treatment, the nonresected and resected groups. The nonresected group consists of thirty-nine cases, in which the treatment was as noted in Table I.

TABLE I. TREATMENT IN NONRESECTED GROUP OF BRONCHIAL ADENOMAS

TREATMENT	CASES
Cautery diathermy alone	11
Roentgen treatment alone	7
Rib resection for empyema followed by diathermy	1
Explored: nonresectable (one of these treated with diathermy and radon later)	2
Diathermy and radon seeds	9
Diathermy and roentgen treatment	3
Diathermy, radon seeds and roentgen treatment	1
Treatment not advised, or advised but refused	5
Total	39

No patient has been treated definitively by bronchoscopic means alone since April, 1948. This is an eloquent expression of the change in opinion of the Mayo Clinic group in regard to the treatment of choice in this condition.

Evidence for Pulmonary Suppuration in the Nonresected Group.—Such evidence is, in this group, clinical only (except for cases in which necropsy was performed) and is not as reliable as in the resected group, in which specimens were available for study. Roentgenographic evidence of severe saccular bronchiectasis or pulmonary abscess, or evidence on bronchoscopy of copious pus flowing from regions distal to the tumor, or both, form the evidence on which Table II is based.

*Positive in that tumor mass was seen or positive biopsy obtained or both.

TABLE II. PULMONARY SUPPURATION IN NONRESECTED GROUP

DEGREE OF SUPPURATION	CASES	
	NUMBER	PER CENT
None to slight	18	46
Moderate	12	54
Severe	9	

Results of treatment in the nonresected group (Table III) are essentially those described by Moersch and McDonald[16] previously. Exclusive of those known to be dead, all except four of the patients in this group were followed four to seventeen years. Twenty-one of the living have been followed five years or more.

Analysis of the causes of death in the ten cases in Table III is very revealing. Seven patients died as a direct result of pulmonary suppuration, or pulmonary suppuration was a major contributing factor in the cause of death. One patient died as a result of a "heart attack," and cause of death is unknown in the remaining two cases.

TABLE III. RESULTS IN THE NONRESECTED GROUP OF BRONCHIAL ADENOMAS

RESULT	PATIENTS
Living at time of last follow-up	25*
Dead	10
Followed less than a year and no recent information	4
Total	39

*Twenty-one followed five years or more; four followed four years.

Resected Group.—The evidence of obstructive pneumonitis in this group is more exact than in the previous group, since the resected specimens were examined in all sixty-three cases. Pulmonary suppuration was none to slight (no changes to airless consolidation without bronchiectasis or any apparent permanent change) in 42 per cent and moderate to severe (bronchiectasis, empyema, abscess, bronchopleural fistula, and so forth) in 58 per cent.

Findings at operation and their effects on ease of procedure are summarized in Table IV. Pneumonectomy was performed in thirty-two cases, and lobectomy or multiple lobectomy in thirty-one cases.

In addition there were two cases in the nonresected group in which exploration, but not resection, was performed, one because of difficulties imposed by

TABLE IV. FINDINGS AT OPERATION AND THEIR EFFECT ON EASE OF RESECTION*

	CASES
No special difficulty†	30
Moderate difficulty‡	14
Great difficulty§	19

*Operation in this group done by Dr. S. W. Harrington, Dr. O. T. Clagett, Dr. H. K. Gray, and Dr. W. D. Seybold. Information for this table taken from the surgeons' notes.

†(1) Filmy adhesions or none; (2) no large inflammatory nodes; (3) minimal hilar induration.

‡(1) Dense adhesions; (2) inflammatory nodes; (3) hilar induration.

§(1) Empyema or pulmonary abscess; (2) thick organized rind of pleura, extremely difficult to dissect, no pleural space; (3) marked fixation and induration of hilus, no landmarks, vessels hard to dissect and to identify.

suppurative disease, and the other because of the mistaken impression that the extensive hilar induration represented a malignant lesion.

Postoperative Complications.—There were ten cases in which postoperative empyema developed. In eight of these ten cases the degree of suppuration in the resected lung and pleural space was moderate to severe. Four of the ten were due to leakage from the bronchial stump with fistula, and in six no definite evidence of fistula was obtained.

In seven of the ten cases hemolytic streptococcus or *Staphylococcus aureus* was obtained. *Escherichia coli* was found in one of the seven cases, and in three cases cultures were negative.

Postoperative Deaths.—There were four postoperative deaths and one death which occurred during a secondary operation eleven months later for empyema. The data on these deaths are as follows:

1. *Right pneumonectomy:* Death five months after operation due to empyema. (No suppuration in resected specimen.)
2. *Right pneumonectomy:* Death at operation because of shock, hemorrhage, and asphyxia. (Very difficult, much suppuration.)
3. *Left pneumonectomy:* Death third day after operation. Collapse of opposite lung. (Slight pneumonitis in resected lung.)
4. *Right pneumonectomy:* Empyema and bronchopleural fistula. Death eleven months later of cardiac arrest during rib resection. (Moderate pneumonitis.)
5. *Right middle and lower lobectomy:* Death due to asphyxia at operation (hemorrhage into tracheobronchial tree). (Moderate pneumonitis, very difficult resection.)

Relation of Degree of Obstruction to Degree of Pneumonitis.—In twenty-one of the sixty-three cases the specimens were sufficiently intact so that reconstruction of the tumor in relation to the bronchial tree could be made. In all these twenty-one, symptoms had been present from one and one-half to fifteen years. Such an examination of fixed specimens cannot of course be totally applicable to the living lung, but in general in specimens with severe degrees of obstruction the degree of pneumonitis was more severe than in specimens with lesser degrees of obstruction. In eighteen cases the obstruction was 50 to 100 per cent, and pneumonitis was moderate to severe in all but one. In three cases obstruction was less than 50 per cent, and pneumonitis was minimal.

There were twelve cases in which the lesions were located peripherally or were arising from a branch of a secondary bronchus only. These fit the description of the five cases described by Maier and Fischer,[17] and in all twelve the symptoms were minimal, the tumor was not visible bronchoscopically, and pneumonitis was minimal.

In general, in cases with symptoms for more than a year, suppuration was more frequent and usually more severe than in cases with shorter duration of symptoms.

Results in the Resected Group.—Exclusive of the three late deaths and the five postoperative deaths, all patients except five were followed one year or

TABLE V. RESULTS OF TREATMENT OF PATIENTS WHO UNDERWENT RESECTION OF BRONCHIAL ADENOMA

RESULT	PATIENTS
Living at time of last follow-up	50
Dead (including postoperative deaths)	8
Insufficient follow-up	5
Total	63

more. Results (Table V) indicate that once diseased pulmonary tissue is removed and the patient recovers from operation there is little danger of trouble from suppurative disease.

Two of the late deaths were due to metastatic malignant lesions, and the cause of death is unknown in the third case.

COMMENT AND CONCLUSIONS

In recent years there has been much discussion as to the degree of malignancy of bronchial adenoma. It has been mentioned, but not sufficiently emphasized, that far more patients with bronchial adenoma have died as a result of suppurative pulmonary disease than have died from metastasis of the adenoma.

Although the antibiotics have made it possible in recent years to control infection and pneumonitis in some degree, their value may be offset by delay in diagnosis of obstructing tumor of the bronchus, if temporary resolution of obstructive pneumonitis occurs on antibiotic therapy, and the physician is not wary of the possibility of obstructing tumor. Our experience has been that, while the antibiotics will control many of the septic manifestations of pneumonitis, they will not prevent the changes in the lung which result from bronchial obstruction.

From the experience at hand it is apparent that approximately 55 to 60 per cent of patients with bronchial adenoma will have significant to severe degrees of obstructive pneumonitis. About 10 per cent of bronchial adenomas will be located peripherally and will produce few or no changes of pneumonitis.

The degree of obstructive pneumonitis appears to be directly related to the duration and degree of bronchial obstruction. The genesis and pathologic characteristics of the changes in bronchial obstruction have been described by McDonald, Harrington, and Clagett,[18] and also by other earlier authors, and these descriptions need no further explanation.

It is of interest to note and compare the results of McDonald, Harrington, and Clagett's study with the present one. If one considers their grade 3 and 4 pneumonitis as comparable to moderate and severe changes, then with their adenoma series some 63 per cent had moderate to severe changes and 37 per cent had no to slight changes. With the squamous-cell carcinoma group, 50 per cent had moderate to severe changes and 50 per cent had no to slight changes. In the large cell carcinoma group 16 per cent had moderate to severe changes and 84 per cent had no to slight changes. In the adenocarcinoma group 21 per cent had moderate to severe changes and 79 per cent had no to slight changes. In the small cell group 27 per cent had moderate to severe changes and 73 per cent had no to slight changes.

These figures are significant in proving the point that the longer the bronchial obstruction is present and the more the degree of obstruction, then the greater the degree of pneumonitis and suppuration. Thus, with the relatively benign (or low-grade malignant) adenoma the incidence of pneumonitis and suppuration is highest, for these patients live longer, have obstruction longer, and obstruction is usually in a centrally located bronchus. Next highest is the squamous-cell group, and the incidence becomes lower the higher the grade of malignancy or the more peripherally the tumor is located.

There seems adequate basis for our belief that surgical resection of the adenomas with severe pneumonitis is much more difficult than resection of adenomas without severe pneumonitis. Actually some of the cases included in this study have been the most difficult of any pulmonary resections. In those cases with marked changes there is extreme difficulty in getting through the dense pleura. The lung may be just a mass of vessels and bronchi with marked

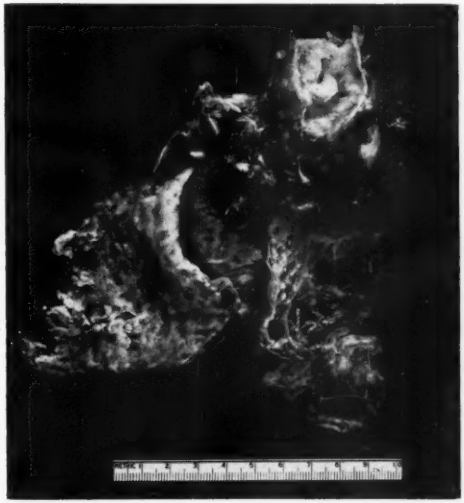

Fig. 1.—Resected lung which had multiple abscesses, dense pleura, and no aerated lung tissue present, all secondary to obstruction by adenoma in the main bronchus.

destruction and inflammation (Figs. 1 and 2). Edema and induration are often of such degree as to make identification and ligation of major vessels very hazardous and difficult. More than half of the resections in the series were difficult because of such reasons.

One extremely interesting observation has been that many of the patients who had severe suppurative lung disease were essentially at times afebrile, many were ambulatory, and some were even working. In this same line, although in several cases large amounts of pus were spilled into the pleural space at operation, not only did empyema not occur, but the patients were afebrile and made uneventful recoveries. We are unable to explain these observations, and unfortunately do not have exact enough data to analyze such cases. In several

cases, however, the pus was found to be bacteriologically sterile, and in others apparently the body had immunized or adapted itself to the presence of such a large necrotic focus. The fact that many of the patients had received antibiotics also undoubtedly played a part in their well-being even when severe pneumonitis was present.

There was a fairly high incidence of postoperative empyema (15 per cent). We believe that obstructive pneumonitis, by increasing the technical difficulties of resection and by the presence of pus, plays a large part in the high incidence of postoperative empyema.

If one considers, however, only those cases in which operation has been performed from 1945 through 1950, the incidence of empyema is only 8 per cent. This compares with an incidence of approximately 11 per cent for empyema following lobectomy and pneumonectomy for malignant pulmonary disease (carcinoma and miscellaneous malignant lesions exclusive of adenoma).*

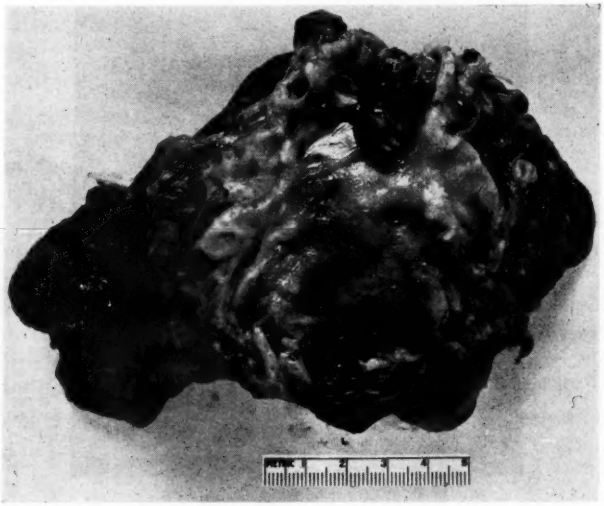

Fig. 2.—Large bronchiectatic cavities in resected lung. These are distal and secondary to bronchial obstruction by an adenoma in the main bronchus.

It is believed that this lower incidence in the case of adenoma in recent years is due not so much to antibiotic and technical changes as to the fact that these patients are now undergoing pulmonary resection early before the severer changes of suppuration have occurred.

Relief of bronchial obstruction by endobronchial resection drainage may be a valuable preoperative procedure in some cases. This has been done in a few of our cases, but not in enough to enable one to draw any conclusions as to its benefit.

*Records of all pulmonary resections for malignant pulmonary disease done at the Mayo Clinic from 1945 through 1950 were reviewed to obtain this figure.

Relief of bronchial obstruction by endoscopic means did, in many cases in the nonresected group, cause relief of symptoms and apparent healing in some cases of severe suppurative disease. However, with recurrence of obstruction severe pneumonitis recurs.

The causes of death in bronchial adenoma also emphasize the importance of the suppurative factor. Of the total group, two patients died apparently as a result of multiple metastatic growths from bronchial adenoma. Exclusive of the postoperative deaths, of the other patients on whom we have adequate information, seven died of pulmonary suppuration and its effects, none of hemorrhage, and one of unrelated causes.

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ADENOCARCINOMA DEVELOPING IN A PERIPHERAL BRONCHIAL ADENOMA

Report of a Case

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ALTHOUGH there is no longer doubt concerning the malignant potentialities of so-called bronchial adenomas, no well-authenticated case of bronchial adenoma showing clear-cut histologic evidence of transition to adenocarcinoma has been recorded. The purpose of this report is to describe and illustrate a case which showed convincing proof of adenocarcinoma developing in a peripheral bronchial adenoma. This observation is of considerable importance in relation to the therapy of patients with bronchial adenoma. It adds further weight to the opinion of those who believe that such lesions should be managed by conservative pulmonary resection, and that endoscopic removal is not an acceptable method of treatment.

Bronchial adenomas may be locally invasive or may metastasize by way of the lymphatics or blood stream.[1, 5] Metastases to the liver, vertebral bodies, opposite lung, and kidney have been reported.[1, 3, 5] In most of these cases the metastatic lesions have been reported as being similar in histologic appearance to the primary tumors, which in turn did not demonstrate microscopical features which would indicate malignant transformation. Graham and Womack[6] expressed the belief that bronchial adenomas may lose their original features and develop into typical bronchogenic carcinomas. They reported a carcinosarcoma of the lung which they believed arose from a bronchial adenoma, but presented no convincing histologic proof for such an interpretation. Holley[3] stated that a case of bronchogenic carcinoma studied at the Army Institute of Pathology presented changes which suggested a histologic transition from bronchial adenoma to bronchogenic carcinoma, but noted that the available material was not conclusive. Clerf and Bucher[7] reported a case of bronchial adenoma in which tissue from the bronchus was examined histologically at intervals over a five-year period at the end of which time carcinomatous change was detected. That finding was confirmed at autopsy. They did not state the histologic type of carcinoma which had developed.

We have seen one or two cases of undifferentiated cell bronchogenic carcinoma which had some features of bronchial adenomas, but the findings were not conclusive. In the case detailed below there seems to be unequivocal evidence of a transition from a carcinoid type of bronchial adenoma to adenocarcinoma.

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The opinions and/or assertions contained herein are those of the authors and are not necessarily to be construed as official or reflecting the views of the Navy Department or the naval service at large.

Received for publication March 24, 1952.

It has been generally accepted that bronchial adenomas are invariably hilar in location. However, Maier and Fischer[8] reported five cases arising from small bronchi with one which was peripherally located. The case described below was also of this rare peripheral variety.

CASE REPORT

Clinical History.—D. L. N., a 32-year-old white man, was first studied in 1945 because of the discovery, on routine chest roentgenogram, of an oval x-ray density in the upper right lung (Fig. 1). All physical and laboratory examinations were within normal limits. Bacteriologic studies of the sputum for tubercle bacilli were negative. He was asymptomatic and afebrile throughout four months of hospitalization. His discharge diagnosis was arrested pulmonary tuberculosis. Subsequent chest roentgenograms taken at six-month intervals showed no significant change until July, 1951, when the mass was found to have enlarged markedly (Fig. 2). The roentgenograms showed the lesion to be well circumscribed, dense, but not homogeneous, and several areas suggested calcium deposition as well as cavitation.

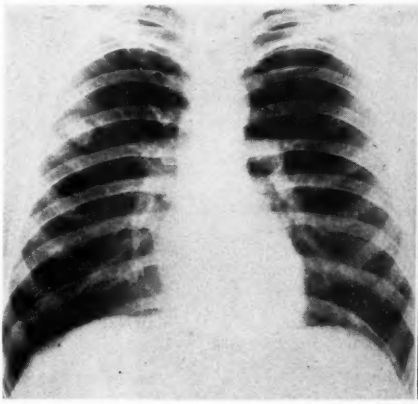

Fig. 1.

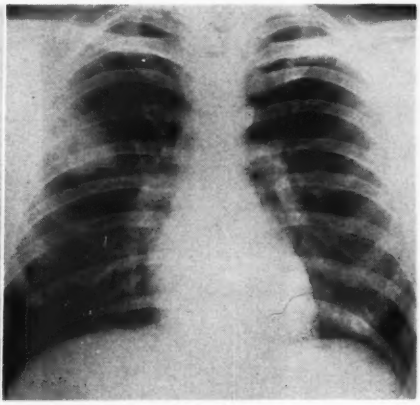

Fig. 2.

Fig. 1.—Roentgenogram taken in 1945, showing the lesion in the peripheral portion of the right upper lung.

Fig. 2.—Roentgenogram taken in 1951, showing the marked increase in size with central cavitation.

He was admitted to the St. Albans Naval Hospital on Nov. 1, 1951. At that time he was still asymptomatic and afebrile, and he remained so during two and one-half months of hospitalization. There was no cough, chest pain, hemoptysis, or sputum production. Breath sounds were slightly diminished, and scattered dry râles were audible in the right paravertebral area below the inferior angle of the right scapula. Second-strength tuberculin skin test was slightly positive. Bronchoscopic examination revealed no positive findings, and aspirated bronchial secretions were negative for acid-fast bacilli and tumor cells.

On Jan. 3, 1952, right thoracotomy was performed. A rounded, moderately firm mass, six centimeters in diameter, was encountered in the posterior segment of the right upper lobe near, but not attached to, the pleura. Frozen sections were reported as "well-differentiated adenocarcinoma" and a right upper lobectomy was performed. The hilar nodes were grossly normal. Nevertheless, several were removed for histologic study. The patient's postoperative course was uneventful.

Pathologic Examination.—

Gross: The tumor consisted of a lobulated, soft, necrotic, spherical mass 5.0 by 6.0 centimeters. Its borders were fairly sharply demarcated but nonencapsulated. The cut surface bulged and presented a massive necrotic center surrounded by soft, friable grayish

tissue. The adjacent pulmonary parenchyma was slightly firmer than normal, and its cut surface was grayish to yellow-brown. Three lymph nodes showed only anthracotic pigmentation.

Microscopic: The tumor pattern varied considerably in different sections and within portions of the same section. It was largely medullary or alveolar with masses of closely packed, small, cuboidal cells with clear cytoplasm and small, round, vesicular nuclei. Small glands or tubules were formed in a few places (Figs. 3 and 4). Stroma was sparse in these regions, and the general appearance was like that of a carcinoid tumor. Elsewhere the cells were slightly larger with eosinophilic or clear mucous-cell type cytoplasm (Fig. 5). Con-

Fig. 3.

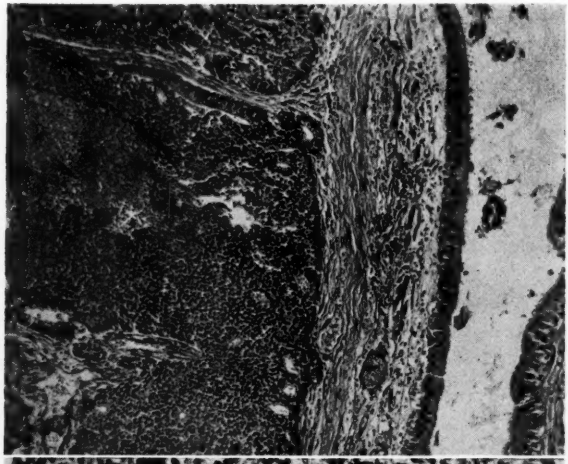

Fig. 4.

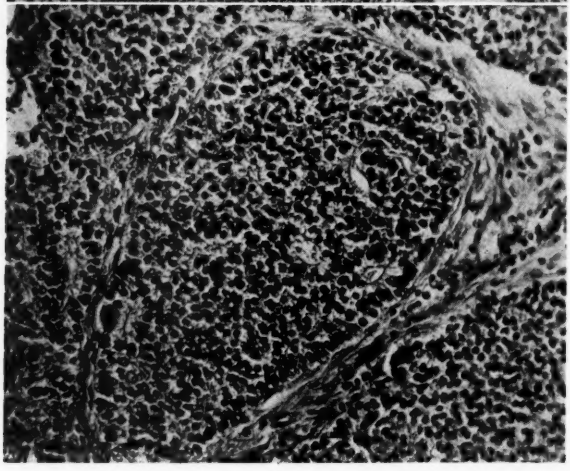

Fig. 3.—Typical histologic appearance of a bronchial adenoma. A few small glands are seen. Note the stroma separating the bronchial epithelium from the tumor. (×50.)

Fig. 4.—Same area under high magnification. Note the strong resemblance to carcinoid tumors. (×125.)

trasting sharply with this appearance was that of other portions of the tumor which presented malignant appearing glandular structures separated by varying amounts of dense fibrous connective tissue (Fig. 6). These glands varied markedly in size and shape and were lined by cuboidal or columnar cells with hyperchromatic nuclei showing considerable anisokaryosis and frequent mitoses (Fig. 7). The benign portion of the tumor appeared to be rising multicentrically from small bronchi or bronchioles. In many places the normal bronchial epithelium could be seen to end abruptly and to widen out into bands of tumor (Fig. 8). Foci of squamous metaplasia were numerous in bronchi within the tumor (Fig. 9). Several lymph nodes were negative for tumor.

Fig. 5.

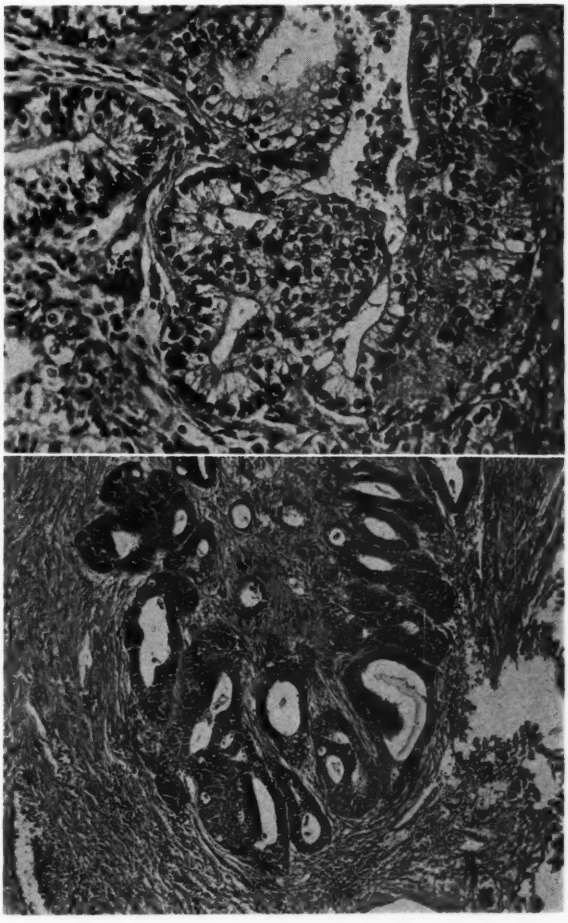

Fig. 6.

Fig. 5.—Area showing tall mucous-type epithelium lining a glandular space and piling up in the lumen. (×125.)

Fig. 6.—Focus of definitely adenocarcinomatous appearance. Note the desmoplastic reaction. (×50.)

DISCUSSION

This case presents several interesting features. The first is the clinical course. The roentgenographic appearance was so suggestive of pulmonary tuberculosis that that diagnosis was still entertained after thorough and prolonged study, despite the absence of symptoms or bacteriologic confirmation. When, six years after its discovery, the lesion suddenly enlarged and developed central cavitation, it was interpreted as indicating extension of a tuberculous process with central necrosis. It seems highly probable that the adenocarcinoma

Fig. 7.

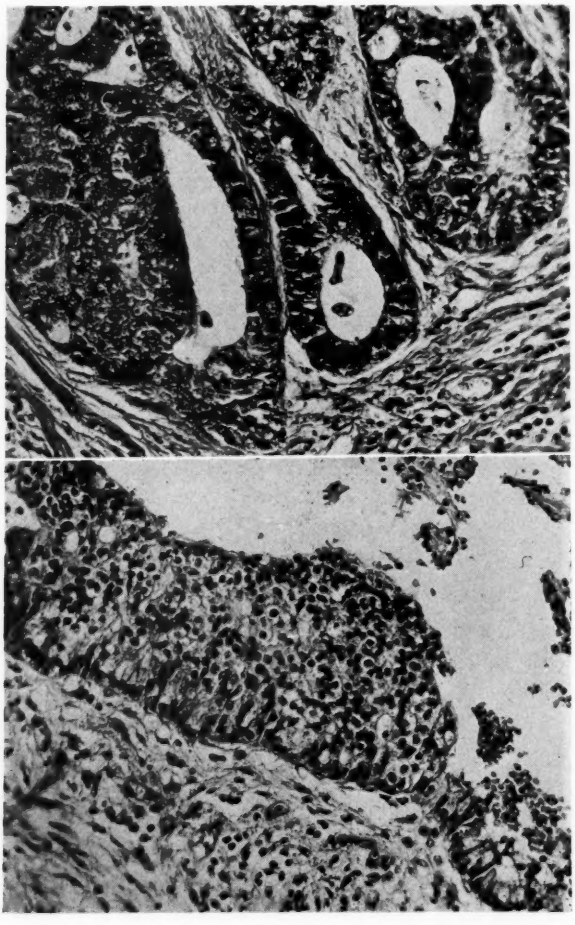

Fig. 8.

Fig. 7.—Same area under high magnification. Compare with benign appearance of Fig. 4. (×125.)

Fig. 8.—Bronchial wall showing junction of normal epithelium and neoplastic tissue which appears to be arising from the lining mucosa. (×125.)

was not present initially, and developed in the adenoma at the time of the rapid increase in size of the tumor. This case is remarkably similar to that reported by Clerf and Bucher[7] which underwent malignant change five years after its detection.

The secondary pulmonary changes usually seen in bronchial adenomas were minimal due to the fact that the tumor was peripherally located, and therefore did not obstruct a large bronchus. The findings in this case agree with those of Anderson[9] who stated that when the diameter of a bronchial adenoma exceeds five centimeters it has been present for at least eight years (as determined from the date of onset of symptoms). The tumor in this case measured six centimeters in its largest diameter and was known to be present at least six years, and probably considerably longer.

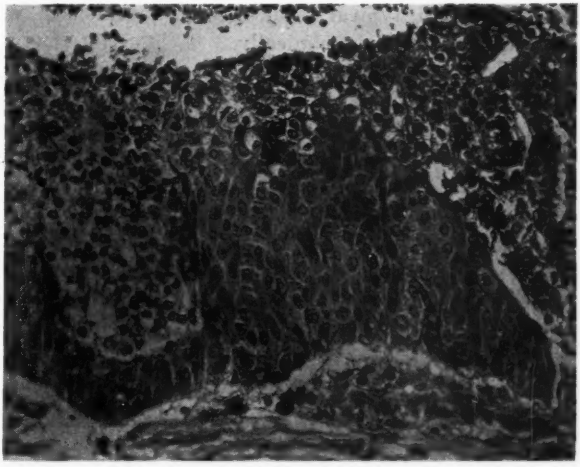

Fig. 9.—Bronchial wall involved by neoplasm and showing an area of squamous metaplasia. (×125.)

In addition to its unusual location and histologic combination, this neoplasm presented still another remarkable feature, that of its apparent origin from bronchial epithelium. This is contrary to most concepts which favor origin from bronchial ducts,[10] bronchial glands,[11] ducts or glands,[12] oncocytes,[13] or undeveloped bronchial buds.[14] The bronchial gland or duct theory has enjoyed the greatest current popularity. This is based chiefly upon the fact that they usually arise from major bronchi and rarely from the smaller rami which do not contain mucous glands. However, transitions from mucous glands to neoplasms have not been reported. The fact that the overlying mucosa is usually intact and separated from the tumor by a band of connective tissue has always mitigated against a mucosal origin. Many authors seem to neglect the fact that bronchial epithelium, as well as bronchial glands, contains mucous-type cells. This case showed definite transitions from normal mucosa to tumor and, while our findings do not disprove the bronchial gland or duct origin, for

most adenomas they do suggest that similar tumors may arise from bronchial epithelium as well. The findings of squamous metaplasia in ducts in the region of the neoplasm has been observed by others.[3, 6]

The histologic changes in this case would seem to provide additional evidence that the term bronchial adenoma is a misnomer. Nevertheless, similar situations are encountered in adenomas of other organs, such as the thyroid or kidney, where a benign-appearing neoplasm may develop into frank carcinoma or may metastasize without any change in its benign histologic appearance. Fatalities due to bronchial adenomas have been due almost exclusively to secondary pulmonary changes, even in those unusual cases with metastases, unless there has been transformation into frank carcinoma. Thus it would seem desirable to retain the term adenoma until a more satisfactory one is found, provided their malignant possibilities are borne in mind. To label them as carcinomas would confuse them with typical bronchogenic carcinomas, which are so dissimilar both morphologically and clinically.

SUMMARY AND CONCLUSIONS

1. A case of peripherally located bronchial adenoma with histologic evidence of transformation into adenocarcinoma six years following its detection has been described.

2. The tumor appeared to arise from multiple foci in the bronchial mucosa.

3. The advisability of retaining the term bronchial adenoma has been briefly discussed.

4. Proved adenocarcinomatous change in a bronchial adenoma further emphasizes the necessity of treating adenomas by pulmonary resection.

5. Finally, cases such as this again raise the question of the acceptability of the policy of "watching" round lesions, thought to be tuberculous in nature.

Acknowledgment: The photomicrographs were taken by Mr. Mort Russin.

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INDUCED PULMONARY TUMORS

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IT IS generally agreed that surgical treatment of carcinoma of the lung is limited by the advanced stage of the disease when it is first seen. More information concerning the etiology of this neoplasm is certainly needed to extend the benefits of surgical therapy and perhaps provide new types of treatment. A study of the causes of experimental pulmonary tumors in animals is one way of approaching the problem, and such an investigation has been made in order to determine whether different agents known to increase the number of these tumors act in a similar manner.

The most useful animal for experimentation on tumors is the mouse, and numerous strains which have been inbred for many generations over a period of years are available for study. The *A* strain is genetically homogeneous and spontaneously develops pulmonary adenomas which are markedly increased in numbers when carcinogenic hydrocarbons,[6] nitrogen mustard,[1, 5, 7] or urethane[10] are administered. Since many other strains are not this susceptible, and the tumors appear regularly from one generation to the next, it is believed that genes for susceptibility to these tumors are present on the chromosomes of this strain. Certain less susceptible strains of mice have visible anomalies each due to a specific gene on the chromosomes. The *W* strain carries three of these mutant genes.

After appropriate crosses between the *A* and *W* strains, the physical appearance and the number and distribution of tumors in the offspring afford sufficient information to tell whether the genes for susceptibility to tumors are linked to genes for the visible anomalies. By comparing results when different chemicals are used to induce the tumors, it should then be possible to tell whether the tumorigenic effects of different chemicals are mediated through a similar pathway. Results of such linkage studies on mice with pulmonary adenomas induced with urethane are presented in this report.

METHODS*

The three mutant genes having visible manifestations in the *W* strain are *shaker-2*,[4] *waved-2*,[9] and *flexed tail*,[2, 8] and are designated as *sh-2*, *wa-2*, and *f*, respectively. All are recessive and must be present on both chromosomes of the pair before a mouse will show the character. Deafness, choreic motions of the head, and occasional whirling movements are caused by *shaker-2*. The coat is curled in the presence of *waved-2*, and the manifestations of *flexed tail* are siderocytic anemia, flexion of the tail, and a white spot on the abdomen. Snell and Law[11] found both *waved-2* and *shaker-2* to be located on the same chromosome. The *A* strain carries the dominant normal genes, *Sh-2*, *Wa-2*, and *F*, at these loci.

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Aided by a grant from the National Cancer Institute, U. S. Public Health Service.
Received for publication April 18, 1952.
*The technical assistance of Betty Cornman is gratefully acknowledged.

Mice of the *A* strain were mated to the *W* strain and the offspring, having one of the genes under discussion from each parent, therefore had the genetic constitution: *Sh-2/sh-2, Wa-2/wa-2, F/f*. Females of this type were then backcrossed to the *W* strain, and among the resulting offspring it was possible to compare *Sh-2/sh-2* to *sh-2/sh-2; Wa-2/wa-2* to *wa-2/wa-2;* and *F/f* to *f/f* individuals. Mice of these genotypes have the following physical appearance, respectively: *Sh-2, sh-2, Wa-2, wa-2, F,* and *f*. This designation will be used in the description hereafter rather than giving the entire genotype.

The animals were injected with urethane at weekly intervals beginning when the mice were ten weeks of age, and continuing for fourteen weeks. One milliliter of recrystallized urethane in 10 per cent aqueous solution was injected intraperitoneally in weekly dosages of 1 ml. per 100 Gm. of body weight. Weights were recorded at weekly intervals throughout the

Fig. 1.—Pulmonary adenoma in the A strain.

study. The mice were autopsied four weeks after the completion of treatment, and the number of pulmonary tumors counted under the dissecting microscope. They were counted again after fixation as a check on the accuracy of the tabulation. Sections were prepared, and histologic study made of the lungs from each mouse. A control group of *A* mice were also given the urethane treatment described and were studied in a similar manner.

RESULTS

Urethane proved to be somewhat toxic in the dosage used, but 91 per cent of the animals survived the treatment. All of those completing 14 injections and surviving four additional weeks were found to have one or more adenomas.

This was confirmed by examination of microscopic sections. The gross appearance of the tumors is illustrated by Fig. 1, and a microscopic section of one of the tumors protruding into the bronchus appears in Fig. 2. In some instances the tumors were exceedingly numerous and involved all lobes of the lung, with a few tumors in some specimens becoming confluent. The number of tumors was checked by weighing the lungs from each mouse. As might be expected, more tumors usually occurred in the lungs weighing the most. There was an average of 34.6 pulmonary adenomas per mouse, with 35.8 in females and 31.2 in males.

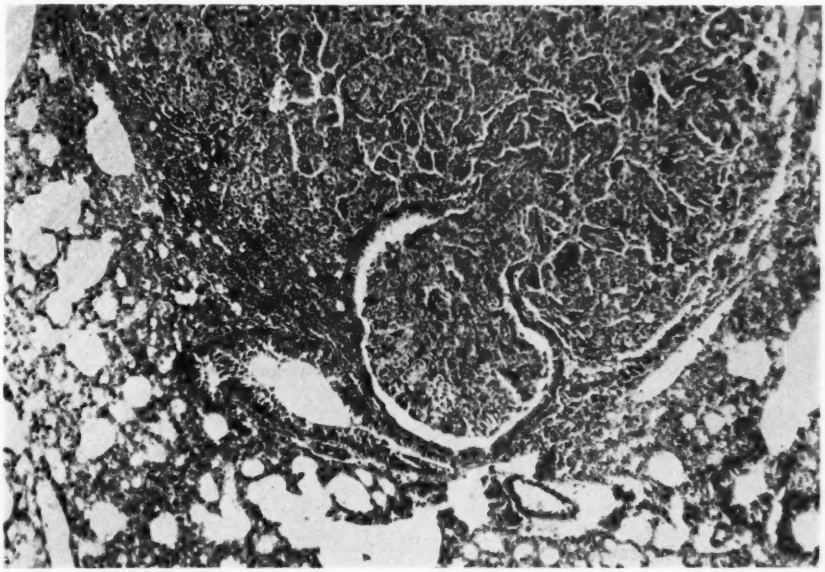

Fig. 2.—Microscopic section of the tumor shown in Fig. 1. Note protrusion of tumor into bronchus.

The mean weight of the lungs was 0.217 Gm. The mean number of tumors in mice with lungs of greater-than-average weight was 45.1, whereas the mean number of adenomas was only 26.0 in those mice with lungs weighing less than the average value. In a control group of 53 mice of the *A* strain, the average number of adenomas per mouse was 83.7, with an average of 85.0 tumors in 30 females and 81.2 tumors in 23 males.

Data for those animals surviving twenty-eight weeks are arranged in Table I so that the tumor count in those mice showing visible manifestations of marker genes may be compared to those without. In the backcross, *Sh-2* mice had an average of 36.1 tumors, whereas *sh-2* animals had only 25.1. This is a statistically significant difference ($P = 0.0001$). Likewise, the average number of tumors, 35.4, for *Wa-2* animals was significantly higher than the average, 25.6, for the *wa-2* group ($P = 0.0007$). On the other hand, the mean number of tumors for *F* (nonflexed tail) mice, 31.1 is not significantly different from the

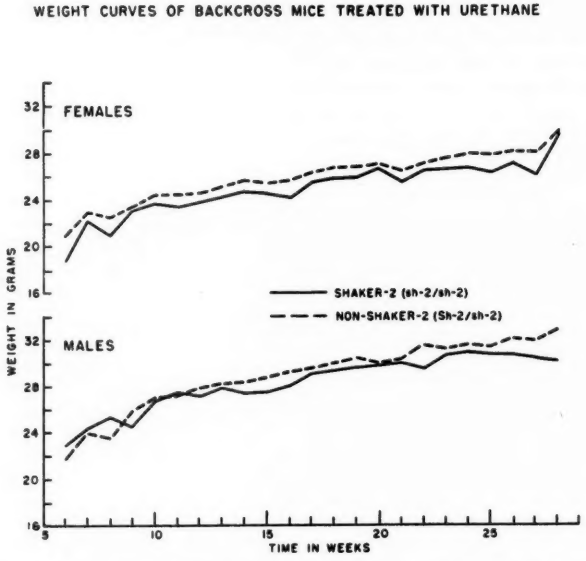

Fig. 3.—Comparison of weight curves of mice with and without *shaker-2*.

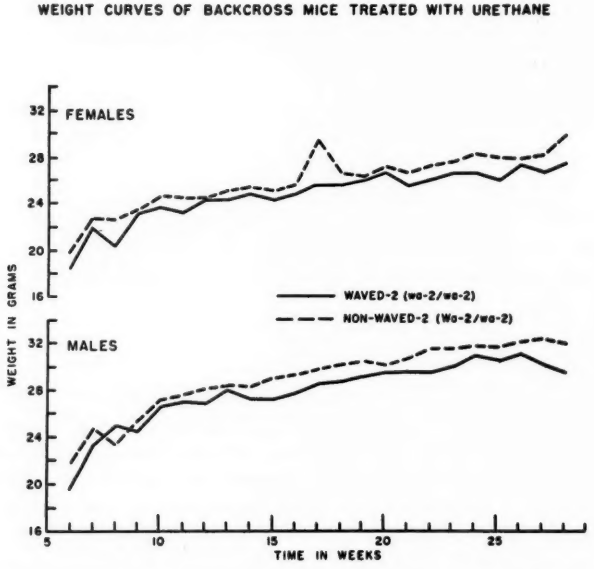

Fig. 4.—Comparison of weight curves of mice with and without *waved-2*.

mean for *f* (flexed-tail) individuals, 32.5 (P = 0.19). Similar differences are found between the medians of the various groups and the means for the right (upper, middle, and lower), right median, and left lobes separately.

Curves for the average body weight of the various groups are shown in Figs. 3 to 6. Although the weights are consistently lower in those mice having *waved-2* coats, *shaker-2* behavior, and a belly spot, the difference is small compared to the range of weights. Females with flexed tails have mean weights very similar to those without, but males with flexed tails have average weights which are less than those with straight tails (Fig. 3).

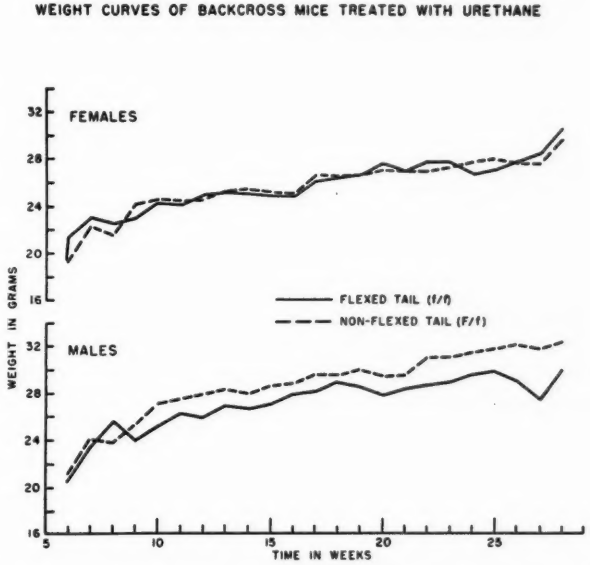

Fig. 5.—Comparison of weight curves of mice with and without flexed tail.

DISCUSSION

There is good evidence that greater numbers of pulmonary tumors appear after urethane treatment when the *Sh-2* and *Wa-2* genes are expressed than when *sh-2* and *wa-2* are present on both chromosomes of the pair (Table I). It is possible that the results for the *Sh-2* and *Wa-2* loci are due to double or secondary effects of each gene, the presence of a susceptibility gene adjacent to each respective marker gene, or the presence of a susceptibility gene (or genes) elsewhere on the chromosome bearing the two markers. Even if only one susceptibility gene were present on the chromosome, the data suggest it to be at a different locus than that associated with *Sh-2* and described by Heston[6] in his experiments with methylcholanthrene. Cowan[3] did not determine linkage, but ascribed susceptibility to one dominant gene when urethane was used for induction of tumors in hybrids of the *A* and *C*^{57} stocks.

Mean body weight is slightly and somewhat consistently lower in groups of mice with the *sh-2* and *wa-2* characteristics, but the difference is not sufficiently large or the corresponding range in weights sufficiently narrow to be considered decisive (Figs. 3 and 4). Also there is a difference between the weights of males and females, and yet the incidence of tumors, if different at all, is lower in males than females. Therefore there is no conclusive evidence that the greater number of pulmonary tumors in *Sh-2* and *Wa-2* mice is secondarily related to the effect of the genes on body weight.

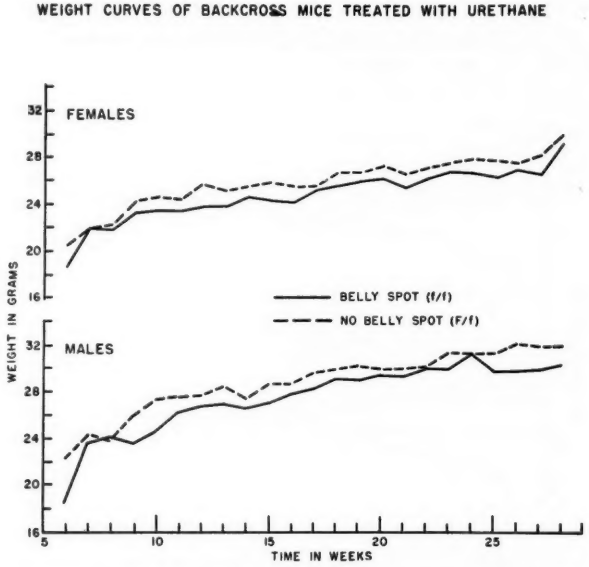

Fig. 6.—Comparison of weight curves of mice with and without belly spot.

No difference is found in the average number of tumors when mice with flexed tails are compared to those without. However, it is interesting that a difference in tumor count becomes apparent as soon as the presence of a belly spot is used as the criterion of the presence of the *f* gene. The decreased incidence of tumors in animals with a belly spot apparently is not an example of true linkage to the *f* gene, but is an association with one of its manifestations. Again the weights encountered do not entirely correspond to expectations if the effect of the gene on tumor incidence is mediated through its effect on body weight. Differences in body weight are small (Figs. 5 and 6) and there is a difference in the weights of males but none in the weights of females when a comparison of the weights of mice with flexed tail and nonflexed tail is made.

Heston[6] reports linkage to *Sh-2* and *F* (nonflexed tail) but not to *Wa-2* when 20-methylcholanthrene was used to induce pulmonary tumors. In contrast to these findings, the data in this report indicate linkage to *Sh-2* and *Wa-2* and

TABLE I. LINKAGE OF SUSCEPTIBILITY TO PULMONARY ADENOMAS INDUCED WITH URETHANE

STRAIN OR GENERATION	MARKER GENES	NO. OF MICE INJECTED	NUMBER OF TUMORS		MEAN TUMORS PER LOBE			
			MEDIAN	MEAN	P	RIGHT†	MEDIAN	LEFT
A		53	84	83.7 ± 2.75*				
BC‡	Sh-2	127	32	36.1 ± 1.92	0.0001	21.6	3.3	11.2
BC	sh-2	97	21	25.1 ± 1.59		14.6	2.3	8.1
BC	Wa-2	132	31	35.4 ± 2.09	0.0007	21.1	3.3	11.2
BC	wa-2	92	22	25.6 ± 2.38		15.1	2.2	7.8
BC	F	179	27	31.1 ± 1.58	0.19	18.6	2.9	9.7
BC	f (Flexed tail)	45	28	32.5 ± 3.38		18.8	2.7	9.8
BC	F	148	30	34.4 ± 1.77	0.003	20.1	3.1	10.9
BC	f (Belly spot)	76	23	25.5 ± 3.58		15.8	2.2	7.6

*Standard error of the mean.
†Upper, middle, and lower.
‡Backcross.

none to *F* (nonflexed tail) when urethane was used. Therefore, the pathway by which the two chemicals act must not be entirely the same, since genes for susceptibility to the chemicals do not show the same linkages.

SUMMARY

1. Resistance to pulmonary adenomas induced with urethane is linked to the *shaker-2* and *waved-2* genes on one chromosome in the mouse but not to the flexed-tail manifestation of an additional gene on another chromosome.

2. Since linkage of susceptibility genes and certain marker genes is not the same for tumors induced by urethane and 20-methylcholanthrene, it is likely that these two chemicals do not act in an entirely similar manner in producing the same type of tumor.

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Announcement

THE AMERICAN ASSOCIATION FOR THORACIC SURGERY

Notice of Annual Meeting

The 33rd annual meeting of the American Association for Thoracic Surgery will be held March 27, 28, and 30, 1953, in San Francisco, Calif. Headquarters will be at the Hotel Fairmont. Suitable accommodations also have been reserved at near-by hotels, the Mark Hopkins, the Huntington and the Sir Francis Drake.

Requests for Hotel Reservations

These should be mailed to Dr. H. Brodie Stephens, Chairman of Hotel Committee, American Association for Thoracic Surgery, Room 200, 61 Grove St., San Francisco 2, Calif. The following information must be included: (1) two choices of hotels; (2) type of accommodation desired—single, double, twin, room or suite; (3) name of other room occupants, if any, whether wife or another doctor; (4) date and approximate hour of arrival; (5) date of departure; (6) return address.

Abstracts for Papers

Abstracts for the presentation of papers at the 1953 meeting must be received on or before Dec. 1, 1952, otherwise they will not be considered by the Program Committee. *Five, repeat, five* copies of each abstract should be sent to the Secretary of the Association, Dr. Paul C. Samson, 2938 McClure St., Oakland 9, Calif. They should not be sent to the Editor.

The abstracts should contain from 200 to 250 words, and should accurately reflect the contents of the completed paper.

Applications for Membership

Applications for Associate Membership in the American Association for Thoracic Surgery must be received by the Membership Committee not later than December 1, 1952, to be considered for action at the meeting in San Francisco in March, 1953. Applications received on a date beyond that deadline must be deferred for consideration until 1954.

Applicants must be sponsored by three Active or Senior Members of the Association. In addition to the sponsoring statement on the application form, the sponsors must submit a separate letter concerning the applicant direct to the Chairman of the Membership Committee. These regulations are at the direction of the Council and were made effective at the meeting in Dallas in 1952.

Completed application forms should be sent to the Chairman of the Membership Committee, Edward M. Kent, M.D., 1406 Clark Building, Pittsburgh 22, Pa.